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SPECIALIZATION WITHIN ROENTGENOLOGY*

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IN RECENT years the problem of specialization in medicine has been intensely discussed. Actually "Specialization" may mean not only the act of specializing, but also the state of being specialized. And "Specialism" is carefully defined in my Webster's dictionary as "Devotion to a branch of knowledge, art or science." Similarly the specialist is "One who devotes himself to a specialty," and finally a "Specialty" is "that for which a person is distinguished, or to which he gives special attention."

Decry it as we may, we are all forced to admit two things about Specialism, first, that we of the medical profession are forced into it by the tremendous accumulation of knowledge in the medical field which no living man now encompasses, and secondly, that the majority of advances in medicine have been made in our generation by the specialist. As Forssell[1] so aptly put it in his address to the Fifth International Congress, "All development in living nature has arisen by progressive subdivision of labor, and by the differentiation of special organs for special tasks, to which must be added, cooperation between those organs." Radiology of today is far too broad a field for anyone but a genius to master. Like the wide fields of medicine and surgery, our requirements are legion and like them we must develop our general practitioners, our consulting specialists, our teachers and research workers and our specialists within the specialty. The general practitioner of roentgenology is called upon for all sorts of work in diagnosis and therapy except the more highly specialized types. The consulting specialist should be freely available to the general practitioner of roentgenology as to his other medical confrères for advice or opinion in the field in which he is most experienced and most interested. The teacher of radiology should have the broadest training and foundation possible, and should be gifted with that native ability to inspire and to stimulate. He should be able to deduce the abstract from the concrete just as wisdom is distilled from knowledge. Our research workers should be our own products, our own pupils encouraged by freedom from financial responsibilities to follow out their own particular paths to wider horizons and greater knowledge. Too often the great advances in roentgenology have been given to us by men outside our field. Cholecystography was given to us by

[1] Forssell, Gösta. The rôle of radiology in medicine. *Radiology*, 1938, *30*, 12–18.

* Presidential Address delivered at the opening of the Forty-first Annual Meeting of the American Roentgen Ray Society, Boston, Mass., Oct. 1–4, 1940.

a surgeon, gastrointestinal studies were initiated by a physiologist, ventriculography and encephalography by a neurosurgeon, urography by a chemist and a urologist, but all of these procedures have been adapted, applied clinically, simplified, and tested by the roentgenologist in cooperation with the appropriate clinician or specialist. Our specialist within the specialty has perhaps the best chance to add to our knowledge and to advance the specialty as a whole. He is the one who, with the broad foundation of a thorough training in all branches of roentgenology, goes on to special proficiency in the roentgenology of one of the organs or systems of the body. His foundation must be broad, for the height of our mental houses of knowledge, like our skyscrapers, is limited by the breadth and solidity of our foundations. He must coordinate and cooperate, for he is the link between the general department of radiology and the special department or clinic which he serves. Without him in radiology the special clinic would take over their own radiological work, a disruptive move which all too often happens when the radiologist is too busy, or too uninterested, or too poorly equipped to do the special work requested.

All of us would like to be considered and treated as "consultants," but the status of consultant cannot be awarded by legislation (as some would have it done), it must be earned. It is said that a commission in the Army automatically makes any man a gentleman but no title or degree or position in Radiology nor even a diploma from the Board of Radiology can qualify any of us as a consultant unless we deserve it. To earn it requires ability, clinical judgment, and personality, as well as plenty of knowledge and experience. These things, plus devotion to his specialty, prepare the way for a successful journey from practitioner to consultant. Availability for consultation is, of course, a prerequisite, so that the roentgenologist who does all of his work in one place has a decided advantage over the one who divides it among several offices or hospitals. I know of one roentgenologist who always entered one of his hospitals by the basement door and "read" his films in a private office so that he would not lose time by having to answer the questions of the other staff physicians! I would consider him merely a film reader and I have often wondered at his standing in our profession. Too often a man's standing is determined more by his popularity or his personality or by the front he puts up than by his ability and his contributions to the specialty, which are the real tests of his worth to humanity.

A full-time position in a large hospital is ideal for availability for consultation, and for concentration of effort. There is a present tendency toward this arrangement which will probably continue until the majority of our members will do their work under one of the many arrangements made possible by modern circumstances. If the hospital is large enough and the type of work diversified enough, there should be division of labor in the roentgen department and concentration of effort in special fields by the director as well as by the junior assistants. I agree with Forssell that the first division should be between diagnosis and therapy as each branch requires widely divergent types of intensive training. If there is enough of each type of work, each might advantageously be made a separate department as has been done in Sweden, perhaps under one administrator for better coordination of effort. For my own part I feel that the roentgen diagnosis section is the more interesting, with its many unpredictable and diversified problems, and more valuable to society with its great potentiality in the early detection of disease and new growths. However, radiotherapy is the only part of our specialty where the doctor-patient relationship is adequately maintained. It is also a field where "optimism seems to vary inversely with the wavelength,"[2] but one in which much good can be done and many things can be discovered. It is not the answer to the cancer problem

[2] Schall, W. E., British radiology in the future. *Brit. J. Radiol.*, 1938, *11*, 767–778.

by any means, but only a temporary stage of alleviation, an occasional cure and a continuous experiment in the application of a poorly understood physical force to the control of an as yet uncognizable biological process. If there are special clinics large enough to require considerable special work, one of the juniors should be encouraged to concentrate upon that particular field until he can give the maximum service, at the same time teaching or giving the still younger men in the department as much as he can of his knowledge and clinical judgment. If the most satisfactory service is not afforded, all too often the specialist will disregard the report of the un specialized roentgenologist (or uninterested one) and make his own interpretations, or form his own subsidiary department under one of his own men. Both eventualities cause great loss of teaching material to the central department. Our motto should be "The Best Service Possible," for after all, even though we are a separate specialty and a very necessary and all-embracing one, we are still a purely ancillary branch to medicine and surgery. Until conditions change, we must maintain our specialty not by building a fence around it, nor by forming a union, with its corollary of coercion, but by as complete a mastery of our own specialty as we can obtain. The roentgenologist who desires to be considered and treated as the equal of his professional colleagues would do well to remember the words of our ex-President Kirklin[3] who said, "Advice which is respectable will usually be respected," and also the aphorism of J. M. Woodburn Morison,[4] "If the man does not dignify the office, the office will not dignify the man."

But to return to my theme of "Specialization within Roentgenology"; may I be so bold as to recommend that the younger men be encouraged to concentrate upon one of the broader subdivisions of Radiology after having acquired as solid a foundation as possible in all of the aspects of our specialty. And may I warn them for you that they must at the same time maintain contact and continue their cooperation with the other work in Radiology, lest they become one of those ultra-specialists who digs himself deeper and deeper into his narrow pit until he thinks the rim of his hole is the horizon of knowledge. A mastery of technique and detail does not constitute a genius, but it is the ability to generalize from the particular which is the hallmark of worth, as Frecker[5] writes. Specializing within the specialty is not the acquisition of new methods and different techniques by one already informed in that field (e.g., the gastroenterologist who decides to do his own roentgenological examinations), but rather the concentration in one field of thought, study and endeavor by one already equipped with a broad foundation of training in roentgenological procedures and principles.

The particular field in which a young roentgenologist may concentrate his efforts may be decided in several ways: (*a*) by fortuitous circumstance such as special opportunity, environment, or pure accident, resulting from association for instance with a pre-eminent brain surgeon, location in a particular section where one disease is especially prevalent, or an epidemic which affords rare opportunity for roentgenological investigation, (*b*) by desire or choice of the individual who has only the average opportunity but more than the average will to learn and who applies it to a certain field, (*c*) by previous training and experience along certain lines, such as pediatrics or orthopedics which made a particular appeal during the internship or residency preceding roentgenological training, (*d*) by cooperation or association with another enthusiastic young specialist of different interest, each bringing his assets and both

[3] Kirklin, B. R. Responsibilities of the radiologist (Presidential Address). AM. J. ROENTGENOL. & RAD. THERAPY, 1937, *38*, 677–680.

[4] Morison, J. M. W., Radiology—its progress and future. *Brit. J. Radiol.*, 1931, *4*, 100–110.

[5] Frecker, E. W. On the importance of the general in the study of the particular: with special reference to radiology. *M. J. Australia*, 1938, *2*, 817–825.

pooling their mental resources and efforts, or, finally, the least happy of all (*e*) by direct assignment of work from the director of the department, to cover a new demand or a fancied deficit in the service. In the first type, certainly no roentgenologist could have avoided learning considerable about brain tumors if he had been associated with a Harvey Cushing, or about silicosis if he lived and worked in the anthracite region of Pennsylvania or about influenza if he were in the roentgen department of a large Army hospital during the terrible epidemics of 1918 or 1919. I could multiply examples and cite names well known to all of you of roentgenologists who have specialized within roentgenology, and who have made important contributions to our knowledge and through that to our own improved ability, men who have become in time the acknowledged masters and referees of their specialty. True, some of them have concentrated too heavily, to the exclusion of all else, and have reached or are approaching that undesirable stage of calcification of the judgment where too much experience brings stiffness and inelasticity, and arbitrary opinion takes the place of wisdom and humility in the face of all that is yet unknown. Nor would I have you think that only the specialist within the specialty can contribute to the broadening of our horizons. The great clinical teachers Hickey, Baetjer, Pancoast, Holmes, and others, have by their personal example, by their lucid expositions in lectures or in textbooks, or by their inoculation of ideals into their intellectual progeny advanced our specialty and added power and prestige to all of our work. The clinical investigators like Caldwell, Pfahler, Stewart, Carman, and others, have helped our forward progress tremendously by their contributions. The research workers trained in Radiology have been unfortunately few and far between but there are promising signs that some of the present generation of young radiologists will be able to carry the torch of knowledge ahead. The physicists associated with radiology have done more than their share of investigative work and deserve all the credit we can give them, but their results have been mostly applicable only in radiotherapy. And in many instances the "general practitioner" of roentgenology has done his share, particularly if he has been honest with himself and with his colleagues, has kept up his interest and his studies and has kept alive that most vital of all prerequisites for success in any field—*The Will to Learn*.

In closing, may I offer the advice to the young men undergoing specialization to build their foundations in radiology as solidly as possible, serve their apprenticeships under the best masters obtainable, and then, when opportunity or choice opens the doors, concentrate their efforts upon one or another promising field within the specialty; but in so doing let them not lose contact with the broad field of radiology nor with their fellow workers lest they suffer the penalties of isolation and the utter confusion of having no one who can understand them. And may I remind the young men of our specialty that the future belongs to them and that it is only through their enthusiasm and vigor that progress can be maintained. While there is still freedom from administrative responsibility, and before age and experience have brought about their inevitable inhibitions and fixations, let the young men of radiology make their new contributions to the medicine of our day. And if they would accept further advice, let them avoid the dissipation of energy which comes from too many committee assignments and from the acceptance of unimportant but time-consuming offices. Let them also write only from accurate observations concerning facts, actions, and reactions and not of generalizations, ideals and trends which is most difficult and unprofitable.

Blackstone Studies, Inc.

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Janeway Lecturer, 1939

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SOME ASPECTS OF THE BIOLOGICAL ACTION OF IONIZING RADIATIONS

JANEWAY LECTURE, 1939*

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I APPRECIATE greatly the honor of being asked to give the Janeway Lecture and I am grateful to those who considered me worthy of it. In honoring me the Society is paying another tribute to Dr. Janeway who was influential in establishing a physical laboratory at Memorial Hospital, and is also honoring my associates and assistants who are largely responsible for whatever contributions to radiological physics the laboratory has made.

It may be of interest to you to know that I became associated with the Memorial Hospital and Dr. Janeway through one of those accidental coincidences which sometimes determine all subsequent events in a man's life. In the fall of 1915 I was a graduate student at Columbia University under Professor George B. Pegram, who was a neighbor and friend of Dr. Janeway. Being able to work with radium had a magic attraction in those days and I accepted a part time position at the hospital. At the time I had no intention of specializing in biophysics, but I soon became interested in the many problems which confronted the radiologist then, and I am still working on some of them.

My association with Dr. Janeway was always very pleasant. He had a lively interest in the physical aspects of radium therapy and we used to discuss current problems at every opportunity. One incident I particularly remember very vividly. Probably you all know that Dr. Janeway died of cancer. The form of radium treatment he received was one that he himself had developed—the so-called "bare tube" implantation method. This treatment can be extremely painful but Dr. Janeway never complained. Finally, after the reaction had subsided, he said to me: "If I get better we must develop a different method; this is too painful." A few months later he passed away. This statement impelled me to develop the "gold seed" method which, at least in part, fulfills Dr. Janeway's wish.

The subject I wish to discuss tonight is very technical and hardly suited for presentation after a banquet such as we have just had. For this reason and in deference to the ladies present, I shall give only an extemporaneous and brief summary of the work, illustrating it at the end by means of a short motion picture.†

In 1937[2] I suggested a preliminary theory of the biological action of ionizing radiations, which admittedly contained many assumptions. In spite of its obvious shortcomings this theory has been of considerable value in suggesting new experiments which have yielded interesting results. In the following paragraphs I shall attempt to expand certain aspects of the theory in accordance with the additional data now available, but other aspects discussed in the 1937 paper will not be considered further at this time. The new experimental data which I shall consider in this paper has been provided by Sugiura's work with mouse sarcoma 180, described in recent publications. I take this opportunity to acknowledge with sincere appreciation my indebtedness to Dr. Sugiura for his valuable cooperation.

Radiation of the type with which we are concerned produces throughout the living cell radio-ions which give rise to chemical changes in the constituents of the cell. Chemical substances may thus be produced

† The full paper which follows was written later.

* Delivered at the Twenty-fourth Annual Meeting of the American Radium Society, St. Louis, Mo., May 15–16, 1939.

which were not present before. Conceivably the presence of the radio-ions may alter the colloidal state of the matter within the cell. It may change the permeability of the cell membrane and nuclear boundary. It may cause genetic changes. In short, it may cause a great many alterations in the cell constituents, but unfortunately we know practically nothing about what really happens at the start. However, we do know that if the dose of radiation is sufficiently large the cell dies. Thus it is obvious that, whatever the *modus operandi* may be, radiation exerts a deleterious influence on the living cell which leads to death if the dose is large enough. It is probable that death is the integrated result of many changes which take place in the cell rather than being due to severe injury of any one component part thereof. Thus, while severe injury of the nucleus could cause a cell to die, there is no very good reason for assuming that the necessary dose of radiation would not injure also, at least to some extent, the cytoplasm, the membrane, etc. If the component parts of a cell are damaged, the consequent derangement of the physiological cell processes must contribute to the final death of the cell. Similarly in a tissue consisting of many cells, changes brought about in the intercellular spaces, directly or indirectly by the radiation, must exert an influence on each individual cell. Finally one cannot exclude *a priori* what might be called the "body reaction" of the individual even if only a part of the body is irradiated. In radiation therapy where one cannot deal with an isolated cell, all these possible influences must be considered.

For many years I have noted that very often the pathologist's report on irradiated tissue contains some reference to the presence of "giant cells" and "swollen nuclei." This indicates that, among other things, radiation has caused an imbibition of water by these cells, as stated for instance by Leo Loeb[5] and Ewing.[1] If water enters the cell it means that the osmotic pressure within its boundary is higher than it is in the surrounding medium. Therefore, radiation must in some way increase the osmotic pressure in the cell. An increase in osmotic pressure may be brought about by: (1) an increase in the number of ions, molecules, and particles, (2) a physico-chemical change which would cause a decrease in the "unbound" water in the cell, (3) both (1) and (2).

There is experimental evidence showing that large organic molecules are broken into smaller units under the action of ionizing radiation (Svedberg and Brohult[10]). This would increase the number of osmotically active particles in the cytoplasm, but since large molecules are also present in the intercellular spaces, it would also increase the osmotic pressure in the medium surrounding the cells. Under these conditions osmotic equilibrium across the cell membrane would not be disturbed appreciably, at least initially. It may be assumed that through diffusion and circulation, the intercellular material would soon be restored to its normal osmotic pressure, while the cytoplasm would retain the radiation-induced higher concentration of molecules and ions for a longer time. An osmotic unbalance across the cell membrane would then result. However, as I pointed out in a previous publication,[2] the increase in ionic and molecular concentrations in protoplasm which may be expected from therapeutic doses of roentgen rays—in the light of our present knowledge—is far from sufficient to account in its entirety for the observed swelling. On the other hand, the number of ions and molecules within the cell could be increased considerably by the radiation in an indirect way. The cell membrane is endowed with characteristic properties of permeability, as illustrated, for instance, by the work of M. H. Jacobs and collaborators. It is only semipermeable and normally it does not allow certain substances to pass into the cell. It is possible that radiation may so alter the permeability of the membrane as to permit the passage of such substances. Heilbrunn and Mazia[4] have pointed out that significant permeability changes do take place under the

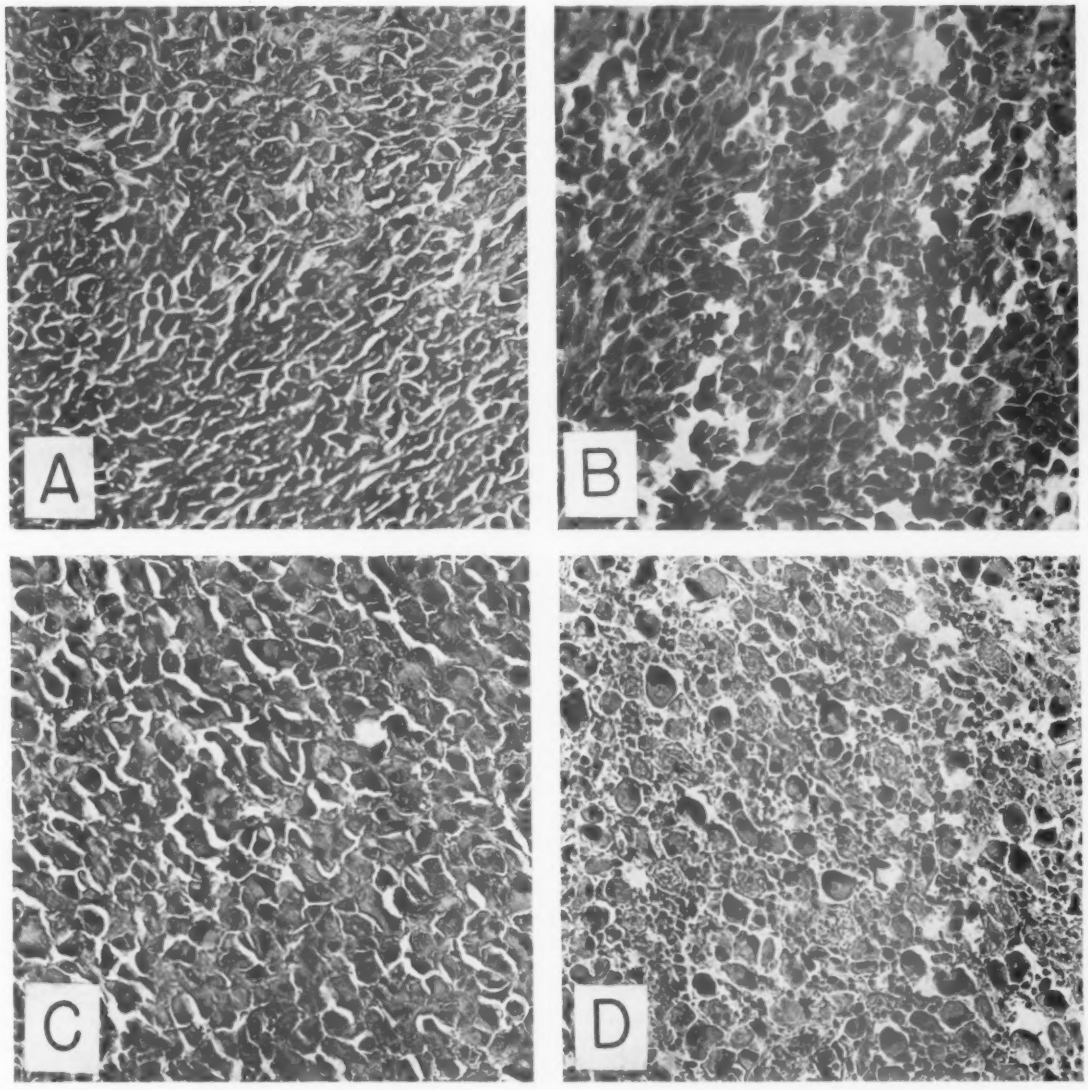

Fig. 1. Showing changes in histologic appearance in irradiated tumors. Photomicrographs of sectioned material were made at the same magnification, 180×. *A*, untreated mouse sarcoma 180; *B*, *C* and *D*, mouse sarcoma 180 irradiated *in vivo* with a dose of 1,500 r and allowed to remain one, three and seven days in the host respectively.

action of radiation. At any rate permeability changes of this nature would increase the osmotic pressure within the cell by increasing the number of ions and molecules in the cytoplasm.

Since it is the *concentration* of ions and molecules which determines the osmotic pressure, it is obvious that an increase in pressure can be brought about by a decrease in the amount of water containing the ions and molecules. This would be the case if the radiation caused physical or chemical changes whereby some water (or its component elements) became part of large molecules already present in the cytoplasm or molecules newly formed by the radiation. For instance hydrophilic colloids may be produced, or in some way water may become "bound" so as not to be available as a solvent. We can conceive, therefore, of three distinct ways in which increase in osmotic pressure within the cell may be brought about by radiation. At this point it may be well to discuss an experiment[8]

which throws considerable light on the phenomenon in question.

Seven day old tumors in mice (sarcoma 180) were administered 1,500 r locally with a small roentgen-ray beam. On the average this dose would cause complete tumor regression in about 90 per cent of the animals. Tumor specimens were then removed at different intervals subsequent to irradiation and prepared for histological study. Figure 1 shows at a magnification of 180 times the appearance of: *A*, untreated specimen; *B*, *C*, *D*, irradiated specimens removed one, three, and seven days after treatment, respectively. The difference in cell size between the unirradiated (control) and irradiated tumors is apparent at a glance. However, the point of greatest interest for the present discussion is the gradual increase in size of the irradiated cells with respect to time. Considerable swelling takes place in twenty-four hours, but it is much greater at the end of the third day. (In the seven day specimen many of the cells have broken down.)

The splitting of large molecules must take place during the irradiation, or at most within a short time thereafter as recombination of radio-ions progresses, owing to thermal agitation and the attraction of ions of different polarities. The removal of radioproducts from the intercellular spaces by circulation can be assumed to take place fairly rapidly, in view, for instance, of the difficulty experienced in trying to keep in a tumor a soluble substance locally injected. Since water can pass freely through the cell membrane, little delay in the onset of swelling can be ascribed to this process. As already mentioned, radiation may alter the permeability of the cell membrane in such a way as to allow the inward passage of substances which are normally kept out of the cell. If this were the case, the amount of such a hypothetical substance which would enter the cell, would depend on its availability outside of the cell—in the intercellular spaces—and would ultimately depend on the replenishment of the supply through circulation. Some delay could be accounted for on this basis. However, the processes just described do not seem sufficient to explain the long period of several days during which swelling gradually increases. Nor can they account for the enormous swelling which the cells attain at the end. After only three days the irradiated cells of sarcoma 180 (Fig. 1, *C*) have an average volume about twelve times that of the non-irradiated cells. One might postulate several hypothetical mechanisms to explain the delay and the degree of final swelling, but since they are not supported by experimental evidence and they seem quite improbable, they need not be described in detail. In this category may be mentioned a change in cell membrane permeability of a reversed unidirectional character, whereby substances which normally remain out of the cell would enter it but could not come out. Similarly one might assume a membrane change which would prevent or greatly reduce the elimination of waste products. From the work of Stanley[7] with tobacco mosaic virus, one might postulate also that radiation sets up in the cytoplasm molecular species with the power of reproduction. Swelling of the cell would then result and would progress gradually as the "raw materials" became available in the cytoplasm by diffusion through the cell membrane.*

Under the microscope the appearance of irradiated cells of sarcoma 180 indicates the presence of considerable water, nevertheless it is not one which might be expected from simple dilution of the cytoplasm. In the case of the cells shown in *C*, Figure 1, such a dilution would have to be in the ratio of 1 to 12 and yet it is evident at a glance that something besides water has accumulated in the cell. Thus the nuclei are greatly enlarged† and are stained just as darkly as those of the control specimen, indicating that they have essentially the

* If this hypothesis were to be entertained seriously it would be necessary to elaborate it so as to take into account the fact that the degree of swelling is related to the dose of radiation.

† The swelling of a nucleus may be considered as a natural consequence of the swelling of a cell. Every process which may be invoked to account for cell swelling may reasonably be applied to nuclear swelling.[2]

same chemical composition. It would seem, therefore, that protoplasmic synthesis has occurred but in an abnormal way. Furthermore, swelling and all the changes in appearance of heavily irradiated cells are on the whole characteristics of degeneration in general and not peculiar to degeneration produced by radiation. Hence, one may well say that radiation damages the living cell, and that swelling and accompanying structural changes are simply manifestations of approaching death of the cell. Obviously, this would make swelling a natural consequence of cell injury and not the cause or one of the causes. While in the ultimate analysis this may be true, we cannot get very far on this basis, since we do not know what the primary injury consists of, or how it occurs. However, one need not take the extreme view that swelling is either the cause or the effect of cell injury. Cell injury leading to death is due most likely to interference with many biological processes caused either directly or indirectly by the radiation. Persistent swelling *per se* should cause some interference, even if it is not very marked at first and is initiated by the direct action of the radiation on some biological entity in the cell.

Whether the swelling of irradiated cells is due to imbibition of water, protoplasmic synthesis or any combination of processes, it is evident that the increase in size can only take place when the necessary materials are first available outside of the cell. Accordingly circulation and diffusion in the intercellular spaces should exert a considerable influence on the swelling of cells, irrespective of the mechanism by which the increase in size is brought about. We shall now examine certain experimental findings from this point of view.

Sugiura[8] has determined the relation between dose and percentage of tumor regressions (sarcoma 180) in mice irradiated locally over the tumor bearing area. This is shown by Curve *A* in Figure 2. In this case "tumor survival" means that the tumor did not regress. Curve *B* shows the relation between dose and percentage of tumor survivals when tumor fragments were irradiated *in vitro*, the criterion of survival being the "taking" of the tumor when inoculated into normal animals.* It will be seen that for a given percentage of tumor survival (e.g., 50 per cent), the dose

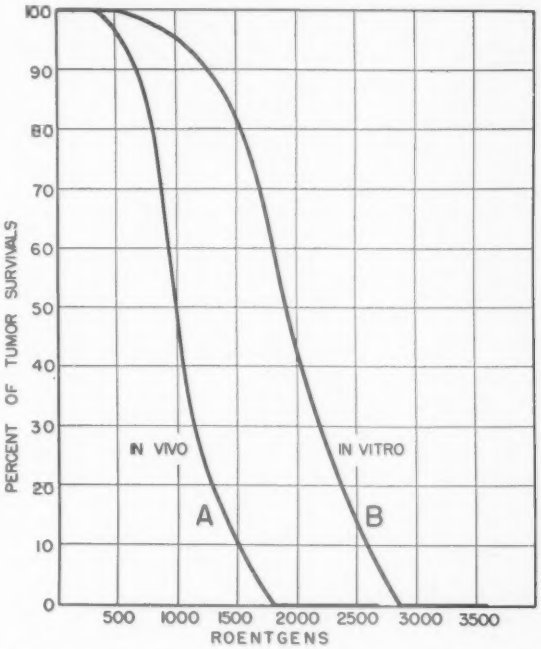

Fig. 2. Survival curves of mouse sarcoma 180 exposed *in vivo* and *in vitro* to 200 kv. roentgen rays, filter 0.5 mm. Cu and 1.6 mm. Al.

in roentgens is almost twice as large for the tumor fragments irradiated *in vitro* as for the tumors irradiated *in vivo*. Provisionally we may conclude from this that the tumor irradiated locally in the animal is subjected to two deleterious actions: (1) a direct one produced by the radiation on the tumor cells, and (2) an indirect one exerted by the tumor bed and the host as a whole. The two are roughly of equal effectiveness since about one-half the amount of radiation is required to kill a certain percentage of tumors *in vivo* as *in vitro*. What is the nature of this indirect action of radiation? In the first place let us see *when* this indirect influence is exerted upon the tumor.

In the same paper[8] Sugiura gives the re-

* The original paper should be consulted for technical details and complete experimental results.

sults of the following experiment: Tumors irradiated in the same way and with the same dose of roentgen rays (1,500 r) were removed from the hosts at different intervals and suitable fragments were inoculated in normal mice in the usual way. The results are shown in Table 1.*

TABLE I

Dose r	Interval between Irradiation (*in vivo*) and Transplantation Days	Tumor Takes Per cent
1500	0 (15 to 60 min.)	80
1500	1	60
1500	3	35
1500	5	20
1500	7	10
2830	0 to 7	0

It will be seen that if the tumor is removed from the animal immediately following the administration of 1,500 r and fragments of it are inoculated into other animals, 80 per cent takes are obtained. Referring to Curve *B*, Figure 2, it is found that this is almost exactly the percentage of tumor survivals (i.e., takes) obtained when tumor fragments are irradiated *in vitro* with the same dose (1,500, r). Therefore, whatever the indirect action on the tumor may be, it is not exerted by the tumor bed and the host during the roentgen treatment.† As the interval between irradiation *in vivo* and transplantation of the tumor into normal mice increases, the effectiveness of the same dose (1,500 r) increases. When the tumor has remained for one week in the host in which it was irradiated and then removed for transplantation, the percentage of takes is only 10 per cent. According to Curve *A*, Figure 2, this is the same‡ as the percentage of tumor survivals when the locally treated tumor is allowed to remain in the host indefinitely. Accordingly the indirect deleterious action exerted on the tumor by the tumor bed and the host is exerted almost entirely during the first week.* Incidentally, when the tumor has received *in vivo* a dose of 2,830 r, the interval between treatment and transplantation is of no consequence—no tumor takes are obtained (see last line in Table 1). The same result is obtained when the tumor is treated *in vitro* with 2,830 r before transplantation (Fig. 2). Evidently this dose is sufficient to prevent subsequent growth even of the most resistant cells of sarcoma 180 whether irradiated *in vitro* or *in vivo*.

In order to throw more light on the problem of the indirect action of radiation on sarcoma 180, Sugiura irradiated small skin areas in normal mice with 1,500 r and then inoculated non-irradiated tumor fragments in these areas (subcutaneously) at different times. When the tumors were inoculated two hours following roentgen treatment of the skin, only about 50 per cent† takes were obtained as compared to 100 per cent for the controls. Implantations made one day later resulted in roughly 60 per cent takes. Those made a few days after the skin had been irradiated gave practically 100 per cent takes. This shows that whatever changes are induced in the irradiated tissues so as to produce an unfavorable terrain for tumor growth are of short duration—a few days. Experiments of this general type and with similar results have been reported by others. Murphy,[6] who has made an extensive study of the subject, attributes the indirect action of radiation on tumors to the large numbers of

* The actual experimental data published by Sugiura show considerable variation. The percentages given here were obtained by plotting the data and drawing what might be considered to be a representative curve to the nearest 5 per cent.

† Of course, this applies only to short treatments, as in the case of the experiments under consideration.

‡ No importance should be attached to the fact that the two figures are exactly 10 per cent. With the large experimental error to which work of this type is subject, the significant thing is that both percentages are small.

* Ewing[1] has emphasized for many years the importance in radiation therapy of the tumor bed reaction to which he attributes growth restraining properties. This is due largely to fibrosis, constriction of blood vessels, etc., which appear later. The indirect action envisaged in the present discussion is of a different type and exerts an influence on the irradiated tumor almost from the start (see Table 1).

† Again the experimental data show considerable variation and one must not attach too much importance to the actual figures given. There is no doubt, however, that the number of takes for tumors inoculated within the first twenty-four hours into irradiated tissue is much lower than in the case of simultaneous controls in each experiment.

lymphocytes found in irradiated tissues. While this may be the correct explanation, an alternative one may be suggested here. In order that a tumor fragment may take, it is necessary that one or more of its cells be able to get food and get rid of waste products within a reasonable time. This means that some sort of circulatory system must be established between the tumor cell or cells and the host, which necessitates the extension of adjoining capillaries. However, it is known that radiation may temporarily inhibit or slow down cell division. Furthermore, other alterations occur in an irradiated tissue. Accordingly, there may be a longer delay in the establishment of circulation or fluid exchange between the tumor graft and the host, when the site of implantation has been previously irradiated. This would make it more difficult for a graft to take and the percentage of successful grafts would be smaller, as shown by the experiment. The fact that such an induced immunity is most marked immediately following irradiation and gradually disappears within a few days lends support to the view just expressed.

It is important to note that this explanation does away with the necessity of invoking some obscure "indirect action" of radiation to account for the fact that tumor grafts do not take so readily in recently irradiated tissue. The radiation has not increased the "resistance" of the host nor has it improved its protective mechanism against tumor growth. It has simply damaged or disorganized temporarily the tissue in which the tumor fragment is placed. The tumor cells are not destroyed by some agent or mechanism set into action by the radiation but they die because the fluid exchange essential to life cannot be established rapidly enough. Sugiura has found that fragments of sarcoma 180 kept on moist filter paper in an incubator at 37° C. lose their viability within a short time. Presumably, the tumor fragment in the animal undergoes similar degenerative changes, although not so rapidly, since some fluid exchange can take place by diffusion before a vascular system is established, as is the case in tissue culture.

Let us return now to the question of indirect action in the case of tumors irradiated *in vivo*. As already stated Sugiura found that sarcoma 180 could be destroyed *in vivo* by approximately one-half the dose of roentgen rays required to kill fragments of the same tumor irradiated *in vitro*. The more marked response of the tumor irradiated in the host points to some sort of indirect action. However, this term implies that the radiation has caused some change in the tumor bed or the host as a whole which is injurious to the tumor. In other words, if we talk of indirect action we must think of something *elicited by the radiation* in tissues or organs other than the tumor itself. We have just suggested in the case of tumor grafts implanted in irradiated tissue that the smaller percentage of takes may be accounted for by the greater difficulty or delay in the establishment of the necessary fluid exchange between the tumor cells and the host. While in a sense this is indirect action, the same mechanism cannot be utilized to account for the greater response of the tumor irradiated *in vivo*. Satisfactory fluid exchange between tumor and host already exists, since the tumor is growing rapidly, and radiation does not interfere with it during the period with which we are concerned here.* On the contrary, we shall attempt to show that good circulation is probably responsible for the greater response of the tumor irradiated *in vivo*.

It will be recalled that for several days following irradiation *in vivo* tumor cells swell to large proportions. Since this involves the intake of water and other substances, it can only occur when there is good circulation in the tumor bed. Now, it has been shown (cf. Table 1) that sarcoma 180 irradiated *in vivo* and then transplanted to normal mice is less viable the longer it is allowed to remain in the host in which it was irradiated. During this period (one week) the tumor cells gradually swell and

* Again we must call attention to the fact that constriction of blood vessels, fibrosis, etc., are "late" reactions.

we, therefore, find the following correlation: Tumors (sarcoma 180) which have been irradiated *in vivo* and have remained in the host for a certain period of time have numerous swollen cells. Fragments of these tumors with swollen cells implanted into normal mice do not grow readily (the percentage of takes is small). On the other hand, under identical conditions, tumor fragments removed immediately after irradiation contain practically no swollen cells and when implanted into other mice produce a large percentage of takes—as large in fact as if the tumor fragments had been irradiated *in vitro*. The greater response of the tumors irradiated *in vivo* and left *in situ* may be attributed, therefore, to the fact that the well established fluid exchange between tumor and host permits the tumor cells to swell soon after the administration of radiation. In the case of tumor fragments irradiated *in vitro* and then implanted, the tumor cells experience difficulty in obtaining the necessary fluids and substances to make them swell, during the time that circulation between the graft and the host is being established. It must be assumed, obviously, that during this time the cells lose something imparted to them by the radiation or that some repair occurs.*

The views just expressed lead to the conclusion that the nature of the medium in which the tumor cells find themselves following irradiation exerts an influence on the cell damage which finally results. Direct evidence in support of this contention—albeit under abnormal conditions—has been provided by Sugiura.[8] Fragments of sarcoma 180 were irradiated *in vitro* with 1,500 roentgens. At the completion of the roentgen treatment equal numbers of fragments were placed in 2 cc. portions of isotonic, hypotonic, and hypertonic Locke-Ringer solutions† in small glass bottles. As controls, non-irradiated tumor fragments were also placed in separate bottles containing the same isotonic, hypotonic, and hypertonic solutions. All specimens were kept in a refrigerator at 4–5° C.* for twenty-four hours and the fragments were then inoculated into normal mice. As an additional control, freshly irradiated tumor fragments (1,500 r *in vitro*) were inoculated at the same time into other normal mice. The average percentage of takes in these controls was 82 per cent which is almost exactly the same percentage as in Curve *B*, Figure 2, for 1,500 r. This shows that the fragments used in these experiments were normal for this type of tumor and responded as usual to a dose of 1,500 r administered *in vitro*. The non-irradiated control fragments kept for twenty-four or even forty-eight hours in the different solutions at a temperature of 4–5° C. produced in all cases 100 per cent takes, showing that immersion in the various solutions, *per se*, had no deleterious effect on the tumor fragments. On the other hand, irradiated fragments which had been immersed in isotonic solution produced only 64 per cent takes, as compared to 82 per cent for the controls (fragments irradiated *in vitro* and implanted immediately). This shows that immersion of the irradiated fragments in isotonic solution for twenty-four hours at 4–5° C. enhanced somewhat the radiation effect. Referring to Table 1 it will be seen that when the tumor is irradiated *in vivo* and is allowed to remain in the host for twenty-four hours before transplanting it to other animals, the proportion of takes is approximately 60 per cent. It would seem from this that such immersion in isotonic salt solution is essentially equivalent to allowing the tumor to remain for the same length of time in the host in which it is

* It is not known whether this can take place in a more or less isolated tissue fragment, but of course recovery from radiation effects does occur in tissues under normal conditions—notably the skin.

† All three solutions contained 0.003 mole KCl and 0.003 mole $CaCl_2$ per liter, but the NaCl content per liter was 0.15 mole for the isotonic solution, 0.12 mole for the hypotonic solution, and 0.18 mole for the hypertonic one. The solutions were buffered to pH 7.4 by adding KH_2PO_4 and KOH.

* At body temperature (which would have been preferable) the tumor does not survive a twenty-four hour immersion in these solutions. It will be seen, however, that in these experiments comparisons are made between irradiated and non-irradiated fragments, immersed in the different solutions, and kept at the same temperature, for the same length of time.

irradiated. However, this can hardly be expected and the close agreement is simply fortuitous. The only important point is that immersion of irradiated tumor fragments in isotonic solution for twenty-four hours at 4–5° C. enhances the radiation effect. The trend is confirmed by additional experiments in which the irradiated tumor fragments were left in isotonic solution at 4–5° C. for periods of forty-eight, seventy-two, and ninety-six hours before implantation, with resultant percentage takes of 60, 50, and 50, respectively. The irradiated tumor fragments kept for twenty-four hours in hypotonic salt solution at 4–5° C. produced on the average 75 per cent takes. This again is lower than the normal average of 82 per cent when the tumor fragments are inoculated immediately following irradiation *in vitro*, but no particular importance can be attached to the exact numerical value.

The results of the remaining experiments are quite striking. Irradiated tumor fragments kept in hypertonic solution for twenty-four hours at 4–5° C. produced 100 per cent takes in all four separate experiments, each consisting of ten tumor implantations. Since the normal average takes for tumor fragments irradiated *in vitro* with 1,500 r and immediately implanted is 82 per cent, the result indicates that immersion in hypertonic solution under the conditions of the experiment counteracts—and apparently wipes out—the radiation effect. This is the more striking when one considers that immersion in hypertonic solution for twenty-four hours is an abnormal procedure which would be expected to be injurious rather than beneficial to the tumor cells. By what mechanism this cancellation of the radiation effect on the tumor fragments is brought about is difficult to visualize. Since immersion of the fragments in hypertonic solution would be expected to remove some water from the cells, one might be tempted to attribute the "loss of radiation effect" to the partial dehydration of the cells. Similarly, the enhancement of the radiation effect by immersion in isotonic or hypotonic solution might be attributed to the possible imbibition of water by the tumor cells. However, these views are apparently contradicted by experiments which will be described presently.

Fifteen irradiated and 15 non-irradiated fragments were weighed before and after immersion for twenty-four hours in isotonic, hypotonic, or hypertonic salt solution, kept at 4–5° C. The results are given in Table II in which are also summarized the results of the other immersion experiments.

TABLE II

EFFECT OF 24-HOUR IMMERSION AT 4–5° C. OF SARCOMA 180 FRAGMENTS ON PERCENTAGE TAKES AND ON WEIGHT. IRRADIATED FRAGMENTS RECEIVED 1500 r *in vitro* PRIOR TO IMMERSION

Type of Solution	Percentage Takes		Percentage Change in Weight Following Immersion	
	Non-irradiated	Irradiated	Non-irradiated	Irradiated
Isotonic	100	64	+3*	+ 9
Hypotonic	100	75	+6	+10
Hypertonic	100	100	−1	+ 8
Without immersion		82		

* It would seem from this figure that the "isotonic" solution was actually somewhat hypotonic. This, however, is irrelevant.

It will be seen that of the non-irradiated fragments those immersed in isotonic and hypertonic solutions gained weight in the order named, whereas those kept in the hypertonic solution underwent a slight loss in weight (1 per cent). This gain or loss of weight had no influence on the viability of the tumor cells since in all cases 100 per cent tumor takes were obtained. The irradiated tumor fragments gained considerable weight (8 to 10 per cent) in *all three solutions*, which would indicate that in all cases water was taken up by the irradiated tumor cells. Yet the radiation effect was counteracted completely in the fragments immersed in hypertonic solution, whereas it was enhanced in those immersed in iso-

tonic or hypotonic solution.* The difference in water uptake is only 1 per cent (from 8 to 9 per cent) between irradiated fragments immersed in hypertonic solution and those immersed in isotonic solution. Gross and histologic examination of tumor fragments after immersion in isotonic, hypotonic, or hypertonic solution, showed no essential difference. One, of course, could not expect to detect swelling of the tumor cells to the slight extent called for by the observed increase in weight (8 to 10 per cent increase in weight corresponds to an increase in diameter of approximately 2 per cent). The more marked increase in weight upon immersion of irradiated fragments as compared to the non-irradiated ones supports the view expressed before that irradiation increases the osmotic pressure of the cytoplasm.†

It is evident that a satisfactory explanation of the results of all the immersion experiments cannot be given at this time. They demonstrate, however, the importance of the part played by the medium surrounding the tumor cells after the radiation has been administered. Apparently the radiation effect (in sarcoma 180) can be enhanced or decreased—and even obliterated—by controlling the tonicity of the medium during a relatively short period following irradiation (twenty-four hours in the experiments). We may say, therefore, that radiation does something to the tumor cell which is potentially injurious. What actually happens to it depends largely on the medium in which it finds itself subsequently. The situation is roughly analogous to the photographic effect: Light does something to the emulsion but the final result depends on the development of the film.

Having found that the characteristics of the medium surrounding an irradiated tumor fragment influence the radiation effect manifested by the tumor, the question immediately arose as to whether one could alter the tumor cell medium in a living animal sufficiently to influence the response of a growing tumor to irradiation. The experimental procedure adopted to test this point is a logical consequence of the views and experimental data presented so far. Sugiura[9] has described the work in a recent publication. Briefly, actively growing, one week old tumors (sarcoma 180) were irradiated locally with roentgen-ray doses ranging from 500 to 1,000 r. Then 0.5 cc. of sterile distilled water was injected into each tumor from one to four times daily for two to six successive days. The results, including those of the control experiments, are given in Table III.

We may point out first that repeated injections of 0.5 cc. of sterile distilled water into 30 non-irradiated tumors, caused no regressions. The results of roentgen treatment alone are in very good agreement with the values shown in Curve *A*, Figure 2. One water injection a day for six days subsequent to roentgen treatment of the tumor had no significant effect. The largest percentages of tumor regressions were obtained when four daily injections were given during the first four to five days following roentgen treatment. Comparison of the tumor regressions obtained by the combined roentgen treatment plus numerous water injections and those obtained with roentgen treatment alone shows a marked increase in favor of the combined treatment. Thus with 500 r, 3 per cent regressions were obtained, whereas with 500 r + H_2O, 36 per cent regressions were obtained. Similarly with 750 r the corresponding figures are, 15 per cent and 61 per cent, while with 1,000 r they are 50 per cent and 93 per cent. It is hardly necessary to point out that as the roentgen-ray dose is increased the two percentages must come closer together, since when the dose is about 1,800 r, roentgen rays alone produce 100 per cent

* The percentages of tumor takes for fragments immersed in isotonic solution (64 per cent) and those immersed in hypotonic solution (75 per cent) are not in the order which one might expect. Of the three sets, the fragments immersed in hypotonic solution should have given the lowest percentage of takes. However, the two are lower than the percentage of takes for the control fragments (82 per cent) which were irradiated *in vitro* and immediately implanted.

† Strictly speaking this statement involves the assumption that the increase in weight of the fragments is due to imbibition of fluid by the tumor cells, whereas liquid may have been taken up by the intercellular material in sufficient amount to account for the entire increase in weight. Lack of experimental data prevents us from settling this point. However, it is reasonable to suppose that the tumor cells did imbibe some if not all the liquid demanded by the increase in weight of the fragments.

regressions. Extrapolating from the last set of figures in Table III, a roentgen-ray dose of 1,050 r, followed by repeated injections of distilled water, would produce 100 per cent regressions. Thus the combined roentgen radiation plus water treatment requires only 60 per cent as much radiation to produce 100 per cent tumor regressions.

slight injury of the tumor cells by distilled water added to that produced by the irradiation could, conceivably, account for the results. Repeated insertions of the injection needle could in themselves be injurious to the tumor. However, the original hypothesis is at least supported, if not confirmed, by experiments in which isotonic, hypo-

TABLE III

EFFECT OF DISTILLED WATER INJECTIONS ON THE REGRESSION OF IRRADIATED MOUSE SARCOMA 180

No. of Tumors Used	Dose in Roentgens	Amount of Water Used at Each Injection (cc.)	No. of Daily Injections	No. of Days Injected	Per Cent of Tumor Regression
30	0	0.5	4	3–6	0
10	0	0.75	2	3–7	10
10	0	1.00	2	3–7	0
36	500	0	0	0	3
20	750	0	0	0	15
40	1000	0	0	0	50
6	500	0.5	1	6	0
6	750	0.5	1	6	17
6	1000	0.5	1	6	33
12	500	0.5	2	2–3	8
12	750	0.5	2	2–3	25
12	1000	0.5	2	2–3	50
16	500	0.5	2	5–6	25
20	750	0.5	2	5–6	45
24	1000	0.5	2	5–6	75
22	500	0.5	4	4–5	36
28	750	0.5	4	4–5	61
30	1000	0.5	4	4–5	93

It will be recalled that the distilled water experiments were undertaken to determine whether the medium surrounding the tumor cells could be altered sufficiently in a living animal to influence the response of a growing tumor to radiation. The positive result obtained does not necessarily prove that the only effect of the distilled water injections on the tumor was an alteration of the medium bathing its cells. Although control experiments showed that injections of distilled water alone produced no regressions, it is nevertheless possible that a tonic, and hypertonic Locke-Ringer solutions* were injected instead of distilled water. The results show that repeated intratumoral injections of isotonic or hypertonic solution, following roentgen treatment of the tumor (500 to 1,000 r as before), had no appreciable influence on the percentage regressions. In other words, the effect of the radiation on the tumor was essentially the same as if no injections had been given. On the other hand, injections of hypotonic solution enhanced the radiation

* These solutions were the same as before.

effect, but not as markedly as injections of distilled water.

All these results are in accord with the hypothesis that the increase in tumor response to radiation is due to a favorable change in the fluid medium around the tumor cells. From the data available thus far it appears that the favorable change consists of a lowering of the tonicity of the medium. In a living animal this can be brought about by injections of distilled water or hypotonic solution, *but only temporarily*, since circulation will tend to rapidly restore osmotic equilibrium. For this reason, the injections must be repeated at frequent intervals to get a marked effect (cf. Table III). Also for this reason, probably, injections of hypertonic solution did not counteract to a detectable degree the radiation effect on the growing tumor—as might have been expected from the results of immersion of irradiated fragments in hypertonic solution.* Of course, if the injections are injurious to the tumor for *some other reason*, the more are given the more marked would be the effect. The point we wish to make in this connection is that, in the absence of any other apparent reason, we are justified in accepting—tentatively—the one which is suggested by the available experimental findings.

It will be noted that all the experiments discussed here have been performed with one type of transplantable animal tumor—mouse sarcoma 180. Even if our deductions are correct in this case, the practical question is whether they apply *in toto* or in part to other types of tumor, and particularly to human tumors. Generalizations based on fragmentary evidence and assumptions are always dangerous and they are especially so in the field of cancer. On the other hand, experience shows that in the past generalizations and hypotheses have greatly accelerated the progress of science. Undoubtedly they can be useful, provided the proper mental attitude is adopted both by those who suggest the generalizations and by those who make use of them. One must always have a clear understanding of the problem and must draw in his own mind a sharp distinction between well-established experimental facts and explicit or implicit assumptions. Furthermore, one must be ready to disregard or modify a hypothesis at any time—which implies that one's mind must be receptive to contradicting evidence.

TABLE IV

EFFECT OF LOCKE-RINGER SOLUTION INJECTIONS ON THE REGRESSION OF IRRADIATED MOUSE SARCOMA 180

Type of Solution	No. of Tumors Used	Dose in Roentgens	Amount of Solution Used at Each Injection (cc.)	No. of Daily Injections	No. of Days Injected	Per Cent of Tumor Regression
Isotonic	6	500	0.5	4	4–5	0
	6	750	0.5	4	4–5	17
	6	1000	0.5	4	4–5	67
Hypotonic	6	500	0.5	4	4–5	33
	6	750	0.5	4	4–5	50
	6	1000	0.5	4	4–5	83
Hypertonic	6	500	0.5	4	4–5	0
	6	750	0.5	4	4–5	17
	6	1000	0.5	4	4–5	50

* The conditions under which the immersion experiments were carried out are so different from those obtaining in tumor bearing animals that a correlation of the two is hardly justified. There is no harm, however, in making use of the results of the immersion experiments to provide leads for further experiments with tumors growing in animals.

There is no place in science for wishful thinking. With these ideas in mind, we shall make the following *tentative* generalizations, to serve as guides for further work. It is hardly necessary to point out that the experimental evidence presented here—or available in the literature—is insufficient to warrant these generalizations. They involve assumptions and extrapolations, which, it is hoped, will not be considered by the reader altogether implausible. The generalizations are not all independent of one another.

Generalization I. The *modus operandi* of the radiation reaction is essentially the same in all mammalian tissues in which the cells and nuclei show a certain characteristic swelling subsequent to the administration of adequate doses of ionizing radiation.

Generalization II. In any given mammalian tissue whose cells exhibit the characteristic swelling reaction, ionizing radiation initiates the swelling process which, coupled with other changes also produced by the radiation, leads to cell death when the dose is sufficiently large.

Generalization III. In any given mammalian tissue whose cells exhibit the characteristic swelling reaction, the extent of cell damage resulting from a given dose of ionizing radiation, depends on: (1) initial changes produced in the cells, and (2) the characteristics of the medium in which the cells find themselves during the swelling period.

Generalization IV. In any given mammalian tissue whose cells exhibit the characteristic swelling reaction, anything in the cells themselves or in the medium, which favors swelling of the cells, enhances the lethal action of ionizing radiation on the cells, and vice versa.

Generalization V. In any given mammalian tissue whose cells exhibit the characteristic swelling reaction, one of the initial changes produced in the cells by ionizing radiation is an increase in osmotic pressure.

Generalization VI. In any given mammalian tissue whose cells exhibit the characteristic swelling reaction, those characteristics of the medium which control the renewal of the fluids bathing the cells during the swelling period have a marked influence on the extent of cell damage resulting from a given dose of ionizing radiation.

Generalization VII. Other conditions being equal, the extent of resultant radiation damage in mammalian cells of the type exhibiting the characteristic swelling reaction is greater the more abundant is the circulation in the immediate neighborhood of the cells during the swelling period, and vice versa.

Generalization VIII. Any means which, acting within physiological limits during the swelling period, increases the circulation in the immediate neighborhood of mammalian cells of the type exhibiting the characteristic swelling reaction, enhances the lethal action of ionizing radiation on the cells, and vice versa.

Generalization IX. Other conditions being equal, the extent of resultant radiation damage in mammalian cells of the type exhibiting the characteristic swelling reaction is more marked the larger the difference in osmotic pressure between the cytoplasm and the medium in which the cells find themselves during the swelling period, and vice versa.

Generalization X. Any means which, acting within physiological limits during the swelling period, increases the difference in osmotic pressure between the cytoplasm of mammalian cells of the type exhibiting the characteristic swelling reaction, and the medium bathing them, enhances the lethal action of ionizing radiation on the cells, and vice versa.

By means of these generalizations one may plan numerous experiments which otherwise would not be obvious. The results of these experiemnts will provide additional data which will either lend support to the generalizations or suggest modifications. Thus eventually one may hope to formulate a theory of the biological action of ionizing radiations with a satisfactory experimental foundation. The generalizations may also be used in the meantime to interpret certain findings in radiation therapy and to suggest possible improvements. In

this connection it should be borne in mind, obviously, that any deductions based on these generalizations are no better than the generalizations themselves, and should be used with great discretion. A few deductions with some practical implications will be discussed in the remaining paragraphs.

Radiosensitivity. According to Generalization III, "In any given mammalian tissue whose cells exhibit the characteristic swelling reaction, the extent of cell damage resulting from a given dose of ionizing radiation, depends on: (1) initial changes produced in the cells, and (2) the characteristics of the medium in which the cells find themselves during the swelling period." Therefore, whether a tumor will respond well to a therapeutic dose of radiation depends not only on the histological (and other inherent) characteristics of the tumor cells, but also on the characteristics of the medium surrounding the tumor cells. Hence, the radiosensitivity which a tumor will actually manifest is the resultant of an *inherent radiosensitivity* pertaining to the cell itself, and *a derived radiosensitivity* depending on the characteristics of the medium.

Referring now to the more specific Generalization VI, we find that "those characteristics of the medium which control the renewal of fluids bathing the cells during the swelling period have a marked influence on the extent of cell damage resulting from a given dose of ionizing radiation." Therefore, among other things, the derived radiosensitivity depends on factors which control circulation (vascular system within and without the tumor, part of body, etc.) and on factors which control diffusion (nature, structure, and distribution of intercellular material).

For dosage and prognostic purposes the actual radiosensitivity of a given tumor under the particular biological conditions in which it exists in the patient constitutes the desired index. It is the resultant of the inherent and derived radiosensitivities as here defined. Obviously it cannot be determined with great accuracy merely by a microscopical examination of a biopsy specimen. This conclusion is in accord with the experience of pathologists who are well versed in the subject. In reality there must be innumerable factors which influence radiosensitivity. Our present intent is simply to call attention to the possible influence of those characteristics of the intercellular medium and tumor environment which control the renewal of fluids bathing the cells, in tumors whose cells exhibit the characteristic swelling reaction to radiation. Since the variables are many, perhaps a better index of the actual radiosensitivity of a tumor in a given case could be obtained from an additional biopsy specimen taken some time after the administration of a "test" dose of radiation. The optimum time interval and the magnitude of the test dose would vary with the characteristics of the case and would have to be determined by experience. This suggestion is made on the assumption that in those tumors whose cells exhibit the characteristic swelling reaction, the presence and appearance of a certain proportion of swollen cells* in the specimen could be made to serve as an additional index of radiosensitivity; and that this could be done early enough in the course of treatment to permit proper adjustment of the therapeutic dose. The feasibility of this suggestion is indicated by the observations of Healy and Arneson.[3]

Radiosensitivity of Metastatic and Recurrent Tumors. Radiologists are familiar with the fact that the primary tumor and its metastases do not always respond equally well to irradiation. No doubt there are many reasons for the difference in response. We should like to suggest as one possible reason that while the inherent radiosensitivity of the tumor is the same, the derived radiosensitivity varies according to the characteristics of the medium in which the tumor is growing. In particular, attention should be paid to circulation and diffusion of fluids not only in the medium surrounding the tumor cells but in the tumor bed as well.

Radiologists have called attention, also,

* Of course, all other radiation changes should be examined with the same end in view.

to the fact that usually tumors which recur after radiation treatment do not respond equally well to a second course of treatment. Apparently the recurrent tumor is more radioresistant. Here again the inherent radiosensitivity of the tumor may have remained constant but the derived radiosensitivity has changed, because the normal tissues in the region have been greatly modified by the previous radiation treatment. It is known in fact that the late changes in irradiated tissue (fibrosis, obliteration of capillaries, etc.) interfere with circulation and diffusion of fluids in the tumor bed, and, consequently, in the medium surrounding the tumor cells.

The foregoing statements—like everything discussed in this paper—are intended to apply to tumors whose cells exhibit the characteristic swelling reaction to adequate doses of ionizing radiation. However, they may have a wider application.

Preoperative Irradiation. The question as to when a tumor should be removed surgically after irradiation has been discussed for many years in radiological circles. Sometimes the view has been expressed that radiation can impart something to the cell only during the time of treatment and if the dose is adequate the cell is doomed, irrespective of subsequent events. This statement would be literally true if in preoperative irradiation one could administer a dose *adequate* to destroy the most resistant cell in the tumor, no matter where it happened to be subsequently. If this could be done there would be no need to operate later. In practice the dose of radiation preoperatively administered can hardly be adequate in this sense.

One of the objects of preoperative irradiation is to prevent, or at least decrease, the occurrence of metastasis, on the assumption that irradiated tumor cells set loose by the surgical procedure or otherwise will not be able to proliferate in other parts of the body. Generalizations III and VI and, more directly, some of Sugiura's experiments with sarcoma 180 are applicable to this problem. It will be recalled that tumors irradiated *in vivo*, immediately extirpated and grafted onto normal animals, showed a much larger percentage of takes than those allowed to remain in the original host for several days before transplantation to new animals. It will be remembered, also, that during this interval the tumor cells gradually swelled to large proportions. To account for the difference in the percentage of tumor takes under these conditions, we have suggested that the medium surrounding the irradiated tumor cells allowed to remain *in situ* for several days favors the early development of the radiation reaction, because there is already a well established circulation at the site of the growing tumor; whereas lack of satisfactory circulation retards the development of the radiation reaction in the cells of tumor fragments irradiated *in vivo* and immediately transplanted to other animals, for a period of time during which the tumor cells lose something imparted to them by the radiation, or partially recover. If the same reasoning can be applied to human tumors whose cells exhibit the characteristic swelling reaction, no operation should be performed until the tumor cells have had time to develop the radiation reaction to a degree sufficient to insure their subsequent death, irrespective of where they may be. The proper interval between irradiation and operation cannot be expected to be the same as for sarcoma 180, and should be determined independently. There are, of course, important practical objections to delaying the operation too long. Therefore, in any particular case the decision on the best time to operate must be arrived at by a judicious compromise.

In the preceding discussion it has been assumed tacitly that irradiated tumor cells which may be disseminated at the time of the operation will find the new surroundings less favorable to the development of the radiation reaction. This is not necessarily true, in view of the results of the immersion experiments, which show that twenty-four hour immersion of irradiated tumor fragments in isotonic solution (at 4–5° C.) was roughly equivalent to allowing the irradiated tumor cell to remain *in situ* in the host for the same length of time.

Therefore, a group of irradiated tumor cells transported to another region at the time of operation may still develop the full radiation effect. If such were the case, the interval between irradiation and surgical intervention would have no influence on the fate of any disseminated tumor cells. However, we have no direct confirmation of this phenomenon, under the conditions obtaining in a living animal, and there is always the possibility that the disseminated cells may lodge in some part of the body where the characteristics of the medium are not favorable to the full development of the radiation reaction. For this reason it would seem desirable to allow the tumor to remain undisturbed, following preoperative irradiation, for as long an interval as is consistent with other considerations in favor of an early operation.

The example just discussed illustrates the care which must be exercised in applying to practical cases the generalizations given here. Whatever conclusions may be reached must be regarded as tentative—as mere suggestions to put to a practical test when, in the judgment of the radiologist, they seem reasonable. It is hoped that in this sense the generalizations and views expressed in this paper will serve to stimulate further research.

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PRESENTATION OF THE JANEWAY MEDAL

At the conclusion of the Janeway Lecture, President W. P. Healy asked Dr. E. H. Skinner to present the Janeway Medal to Dr. Failla. This Dr. Skinner did in the following speech of presentation:

This medal in bronze represents the god, Odin, seeking wisdom from Mimir who guarded the well of knowledge. Mimir insisted that the sacrifice of some portion of his body was required in order to obtain a potion of wisdom. Odin gave his right eye. Upon the obverse of the medal there are two ravens. These birds perched upon the shoulders of Odin. Each morning they ventured forth into different parts of the world in order to find some new piece of information, some new item of wisdom; possibly some news behind the news. Each evening they returned with these useful items to add to the knowledge of Odin.

Gioacchino Failla, Doctor of Philosophy: Quiet, industrious, thorough. Gifted in the imaginative and analytical processes and the extensions of the physical principles of radioactivity applicable to the clinical manifestations of disease in man. His practical approach to the liaison between the physics and the clinical problems of cancer provides a lengthening shadow upon the history of radiation therapy as recorded in the annals of the American Radium Society.

To you, Gioacchino Failla, this Society conveys this bronze token to commemorate the Janeway Lecture. May you continue to hurl this disc and smash the atoms within the darkness of the physical future. May you bring forth more and more to the everlasting benefit of those who will continue to honor your work and your name!

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ADOLESCENT DEVELOPMENT OF THE SELLA TURCICA AND THE FRONTAL SINUS BASED ON CONSECUTIVE ROENTGENOGRAMS

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I. DEVELOPMENT OF THE SELLA TURCICA

IT HAS been known for some time that the sella turcica, enclosing the delicate pituitary gland, though imbedded in the sphenoid bone in the midst of the basicranium, grows with the body as a whole. This conclusion has been based on mass statistics. It has been thought worth while to consider the changes that occur in the sella in the same child in successive years, and to tie them up, if possible, with growth changes of the individual.

a. Statement of Problem. As stated, the earlier studies on sella growth have not been made by individual, longitudinal studies. One of the earliest was made by Hrdlička[5] on dried adult skulls. He measured length, width and depth of the sella and divided the sum of these dimensions by 3 to obtain a "modulus." There was no clear relation between the modulus of the sella and the circumference of the skull.

Gordon and Bell[3] measured length and height of the sella from roentgenograms of boys and girls of ages one to twelve, 3 to 13 heads for each year. They found a slight increase in size of the sella from the youngest to the eldest; but no measurable relationship between the size of the head and size of the sella. They concluded that the sellas of girls are longer and higher than those of the boys; but it is doubtful if the difference found by them is statistically significant.

One of the most complete studies on this topic is by Steiert[12] who, from roentgenograms of 165 normal children between the ages zero and sixteen years, found the area of the sagittal section to increase rapidly from 15 sq. mm. at birth to 56 at one to four years. Between that age and eleven years in girls and thirteen years in boys very little growth occurred; but after that the area rises within three to five years to about 87 sq. mm. The ages of beginning rapid increase are about one year earlier than the mean ages of the adolescent spurt of growth. Studies by Maier[8] confirm the results of Steiert.

b. Material and Method. Our studies are based on roentgenograms of the heads of 46 boys and 50 girls at Letchworth Village, made at the birth month during the years 1932 to 1937 inclusive, beginning when the children were from ten to fourteen years old, so that the age extends, for the most part, until ages fifteen to eighteen had been reached. The children were of various European and American stocks. North Europeans and mixed, Italian, Jewish. Five boys and 7 girls were American Negroes. Not all of the roentgenograms could be used. Available were 13 pairs with one year interval and 31 pairs with a two year interval. It seemed necessary to reject data based on intervals of three or more years.

The roentgenograms were taken by one of us (O. R.). The technique was as follows: All roentgenograms of the skull were taken at a distance of 30 inches and the central ray centered half way between the outer canthus and the auditory meatus. They were taken on a curved Potter-Bucky diaphragm with a 25 inch radius. This raises the head about 1 inch above the roentgen film and may help to account for the variation between the measurements of the roentgenogram and the actual measurements of the head. Another reason for the difference may be the improper positioning of the

head when taking roentgenograms. The head was placed so that a line drawn between the eyes, down the ridge of the nose and through the center of the lips and chin was parallel to the edge of the table. An imaginary line across the top of the head was also parallel to the table. It would be easy to make an error in judging these things parallel and thus make some difference between successive measurements.

A comparison of the head length of a child with that of his roentgenogram taken in the same month tells us that there is an increase in the length of the head on the roentgenogram over nature of between 15 and 20 per cent. The increase of the sella shadow is, of course, much less than that since it lay in the center of a plane that was normal to the incident ray. It is, indeed, 2.5 per cent. This increase was determined by making a roentgenogram of a cent at the appropriate distance from the film.

In comparing successive films of the same individual, the principal sources of error are vagueness of the roentgenograms (especially in some of the earlier ones), foreshortening by inclination of the sagittal plane from normal to the ray. Such foreshortening can usually be detected by measurements of total head dimensions of the roentgenogram. When the roentgenograms were unsatisfactory the outlines obtained from them were discarded.

As a basis of measurement of the sagittal sections of the sella, and after a study of sectioned dried skulls and of published roentgenograms, a tracing of the outline of the sella was made on tracing cloth. The area of the cross-section as thus traced was limited above by a line drawn tangent to top of the dorsum sellae and normal to the tuberculum sellae or at its angle when one is present.

As a check on the adjustment of the head normal to the incident ray, the maximum head length from glabellar region (usually the frontal sinus) to the occiput was measured. If in the series of exposures the maximum head length as measured on the film was 5 mm. or over less than on the preceding exposure that film was excluded from consideration of the changing size of the sella.

The area of the cross-section of the sella thus delimited was measured by the senior author and his assistant, Mr. Wilfred D. Hallock, by means of a planimeter, at least 4 times, and more frequently if the results were discordant.*

c. Results. Table 1 gives the sizes in square millimeters of sagittal cross-sectional areas of the sella turcicas obtained from roentgenograms of children fifteen years of age, unadjusted.

TABLE I

AREAS OF SECTION OF SELLA TURCICA OF CHILDREN 15 YEARS OLD

Area sq. mm.	Male	Female
30.0– 39.9	—	1
40.0– 49.9	—	0
50.0– 59.9	2	1
60.0– 69.9	5	5
70.0– 79.9	6	5
80.0– 89.9	5	3
90.0– 99.9	2	3
100.0–109.9	0	6
110.0–119.9	2	6
120.0–129.9	0	3
130.0–139.9	1	1

The mean of the male series is 81.087 sq. mm. ∓ 4.020†; of the female series, 92.941 sq. mm. ∓4.072. There is thus a barely significant difference between the sexes. Royster and Moriarty[12] find the sella slightly smaller in the female. Some idea of the variation in form and size of the sellas of different children may be gained by an inspection of Figures 3 and 4.

The distribution of changes in square millimeters of the cross-section of the sella turcica in passing from one birth month to the next following in which the sella could be measured is given in Table II.

From this table it appears that of the 91 tracings of males the mean change in a mean interval of 1.3 years is 6.25 ∓ 1.49 sq.

* Grateful acknowledgment is made to Mr. Harry Tappen, Supervisor of the Town of Oyster Bay, for arranging for the loan to us, for this work, of a Keuffel and Esser planimeter from the tax map office of the town.

† The standard error is used throughout this paper.

TABLE II

GIVING THE NUMBER OF CASES OF THE GIVEN CHANGE IN AREA OF CROSS-SECTION OF SELLA TURCICA FROM ONE OBSERVATION TO THE NEXT FOLLOWING ONE

Class Values	−32.5	−27.5	−22.5	−17.5	−12.5	−7.5	−2.5	+2.5	+7.5	+12.5	+17.5	+22.5	+27.5	+32.5	+37.5	+42.5	+47.5 sq. mm.
Male	1	1	3	1	1	10	7	18	20	12	4	3	3	4	2	0	1
Female	—	—	—	3	4	17	16	17	21	20	11	4	6	3	1	1	0
Male and Female	1	1	3	4	5	27	23	35	41	32	15	7	9	7	3	1	1

mm. and of the 124 tracings of females the mean change is 6.49±1.09 sq. mm. For both sexes combined (since the sex difference is not significant) the mean of 215 tracings is 6.30±0.90 mm. Median 6.04 mm.

From Table II it appears, first, that not all of the changes are positive. There are two possible explanations for this: (1) The orientation of the head is faulty; has turned out of the perpendicular to the incident ray; or it may be that in other respects the successive roentgenograms have not given entirely comparable pictures. (2) The cross-section of the sella has actually contracted. Naturally the fact of the difficulty of precise orientation leads one to suspect that some of the negative changes are due to that difficulty. However, the second possibility must be kept in mind. For the living bony structure is really a plastic, changing thing, and can readily adapt itself to changes in size of the vascular body it surrounds. In the case of pituitary tumor the sella becomes much enlarged. Of interest are the following constantly diminishing or at least not increasing series of sella areas expressed in square millimeters (Table III):

TABLE III

FOUR SERIES OF DIMINISHING SIZE OF SELLA TURCICA IN SUCCESSIVE YEARS

Name	Year: 1933	1934	1935	1936
Samuel But.	—	77.4	71.5	61.2
Marion Camp.	45.7	38.7	38.7	35.5
Joseph Gar.	86.9	77.4	83.9	83.9
Pearl Sur.	73.5	—	68.4	63.1

It must be said that these are small values for the cross-section of the sella. Values between 100 to 150 are the more commonly found. The possibility of an occasional shrinkage with age of the hypophysis and its enveloping sella is an hypothesis that should be kept in mind (see Figs. 1 and 2).

For comparison we give four wholly positive series of cross-sectional areas in square millimeters (Table IV).

The conclusion seems justified that the

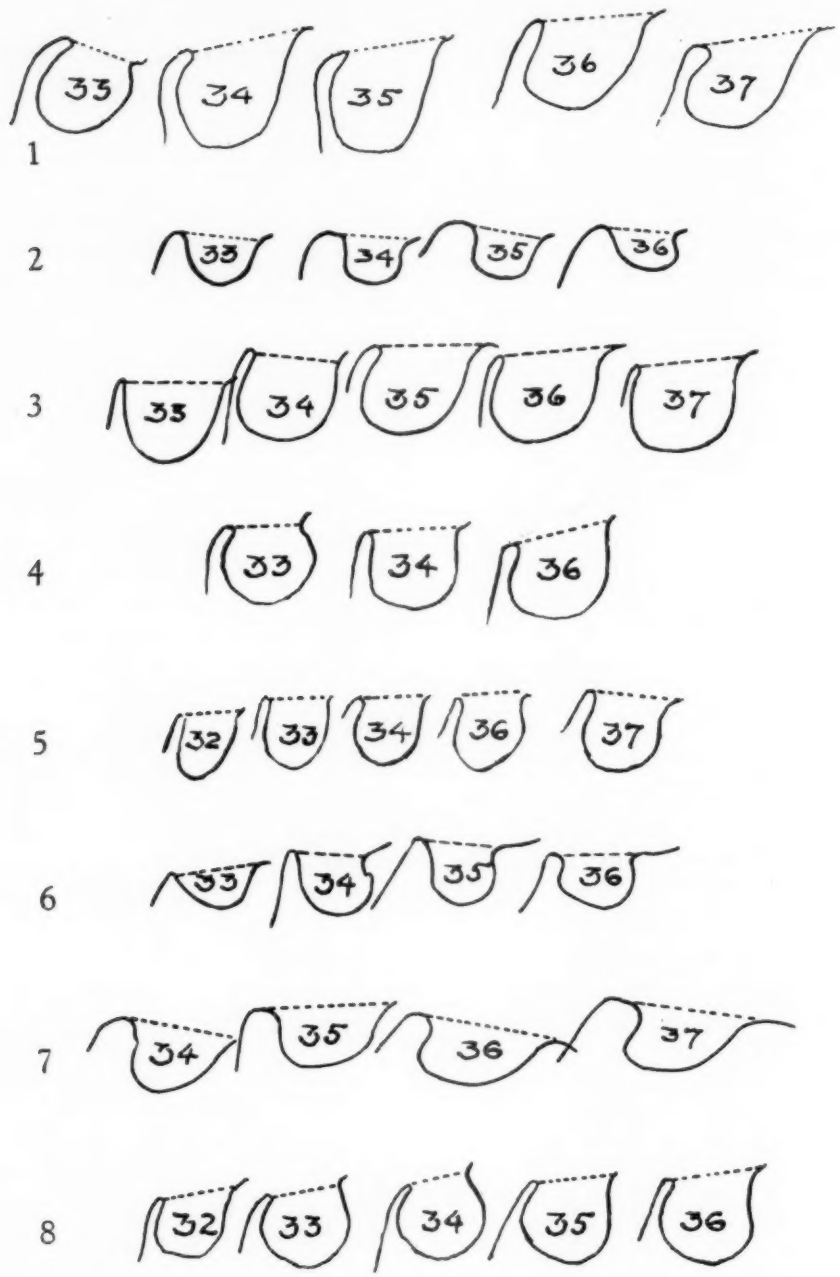

FIG. 1. Outlines of sella turcica (natural size) in successive years of 8 persons as follows:

1. Large type: G. W., male. 1933, 93.5 sq. mm.; 1934, 114.2 sq. mm.; 1935, 149.0 sq. mm.; 1936, 151.6 sq. mm.

2. Small and decreasing type: M. C., female. 1933, 45.7 sq. mm.; 1934, 38.7 sq. mm.; 1935, 38.7 sq. mm.; 1936, 35.5 sq. mm.

3. Median type: B. M., female. 1933, 103.2 sq. mm.; 1934, 112.9 sq. mm.; 1935, 135.5 sq. mm.; 1936, 141.9 sq. mm.; 1937, 132.2 sq. mm.

4. Rapidly growing type: J. D., male. 1933, 98.6 sq. mm.; 1934, 109.6 sq. mm.; 1936, 122.5 sq. mm.

5. Deep-narrow type: J. M., male. 1932, 54.8 sq. mm.; 1933, 63.2 sq. mm.; 1934, 61.2 sq. mm.; 1936, 77.4 sq. mm.; 1937, 78.0 sq. mm.

6. Shallow type: E. B., male. 1933, 36.7 sq. mm.; 1934, 64.5 sq. mm.; 1935, 56.0 sq. mm.; 1936, 56.7 sq. mm.

(*Legend concluded on next page.*)

cross-section of the sella turcica tends to change with age, and, indeed, on the average, to enlarge about 5 sq. mm. per annum.

Since secretions of the anterior pituitary body (pars anterior) which occupies a large part of the sella turcica influence growth of the body as a whole, the hypothesis may be entertained that there is a relation between size of the sella turcica and size of whole body.

To test this hypothesis the correlation was computed between the area of the cross-section of the sella and the body weight, taken at the same time. The result is, for males, $r=0.470\mp0.201$; and for females $r=0.327\mp0.190$. Thus, there is apparently no significant correlation between the values of these two quantities. More striking than the correlation coefficient is the fact that the girl, M. C., who had the smallest sella (35.5 sq. mm. cross-section) had also the smallest body weight (37.42 kg.) at last measurement. Also the 3 boys with smallest sellas are all below standard in weight. Again, the boy, A. D., who had the largest sella (174.2 sq. mm. cross-section, at sixteen years) had the greatest weight of all the children. The low correlation coefficient found is due to a large scattering in the middle groups of sella turcica area and weight. It seems to us that the results justify the conclusion that, contrary to the findings of Gordon and Bell,[3,4] at extremes at any rate there is for post-adolescents a real positive correlation between size of sella turcica and general body weight at the same age.

Another question that arose is: Is there a correlation between the increase of cross-sectional area of the sella turcica during any year and amount of increase in weight during that year? Computation shows that for males this amounts to $r=-0.234\mp0.55$. This negative value is partly due to the scatter of increase of weights when increase of sella turcica is negative. But if these negative increases be eliminated, the coefficient of correlation is still close to zero. In the case of females the value of $r(=0.1740)$ is still small compared with the standard error, ∓0.1320.

It is, of course, quite possible that the increase of the sella is more strongly correlated with increase of weight during the following year and so the appropriate computations to test this hypothesis were made with the following results:

CORRELATION BETWEEN SELLA AREA INCREMENT AND WEIGHT INCREMENT, FEMALES

3 months later	0.0998 ∓ 0.1360
6 months later	0.1248 ∓ 0.1341
9 months later	0.0412 ∓ 0.1361
12 months later	0.1932 ∓ 0.1310
18 months later	0.1749 ∓ 0.1319

It thus appears that increments in weight for twelve months later than the increments

Table IV

FOUR SERIES OF INCREASING SIZE OF SELLA TURCICA IN SUCCESSIVE YEARS*

Name	Year: 1933	1934	1935	1936	1937
Mary Sie.	105.8	110.9	114.8	118.7	126.4
George Wil.	93.5	114.2	146.4	149.0	151.6
Mable Hol.	88.2	108.2	116.1	130.1	—
Lena Dru.	79.2	93.4	103.2	105.3	129.0

* The following notes concerning the personality of the persons mentioned in Tables III and IV are offered:

With decreasing size of the sella, Samuel's I.Q. fell from 60 in 1934 to 49 in 1937. He is untidy, loud, and does not get along well with boys. Has done no academic work. Marion's I.Q. decreased from 49 to 28. She is stubborn, subject to convulsions; steadily deteriorating. Joseph's I.Q. fell from 32 to 28 in three years. He is restless, untidy, inefficient, readily falls asleep. Pearl's I.Q. decreased from 49 to 33. She is slow, seclusive, tidy; has done poor work in school. Lacks persistence. Behavior good.

With increasing size of sella turcica, Mary's I.Q. fell from 50 to 44. She is stupid, untidy, very talkative. She did fair work in low grades at school. George (colored) increased in I.Q. from 66 to 72. He is a good energetic worker, does good work with the trucks; sociable. Mabel's I.Q. decreased from 40 to 38. She is quiet, clean, friendly and talkative. Does good needle work. Lena's (colored) I.Q. fell from 70 to 57. Sociable, active, did fairly good work in the beginning grades at school.

All 4 of those with decreasing sellas are socially defective. Of the 4 with increasing sellas all are of a higher grade emotionally and socially than those with decreasing sellas.

7. Broad shallow type: R. B., female. Am. Negro. 1934, 80.6 sq. mm., 1935, 83.9 sq. mm.; 1936, 92.2 sq. mm.; 1937, 93.8 sq. mm.

8. Round type: A. S., female. 1932, 65.1 sq. mm.; 1933, 93.5 sq. mm.; 1934, 94.2 sq. mm.; 1935, 108.4 sq. mm.; 1936, 114.8 sq. mm.

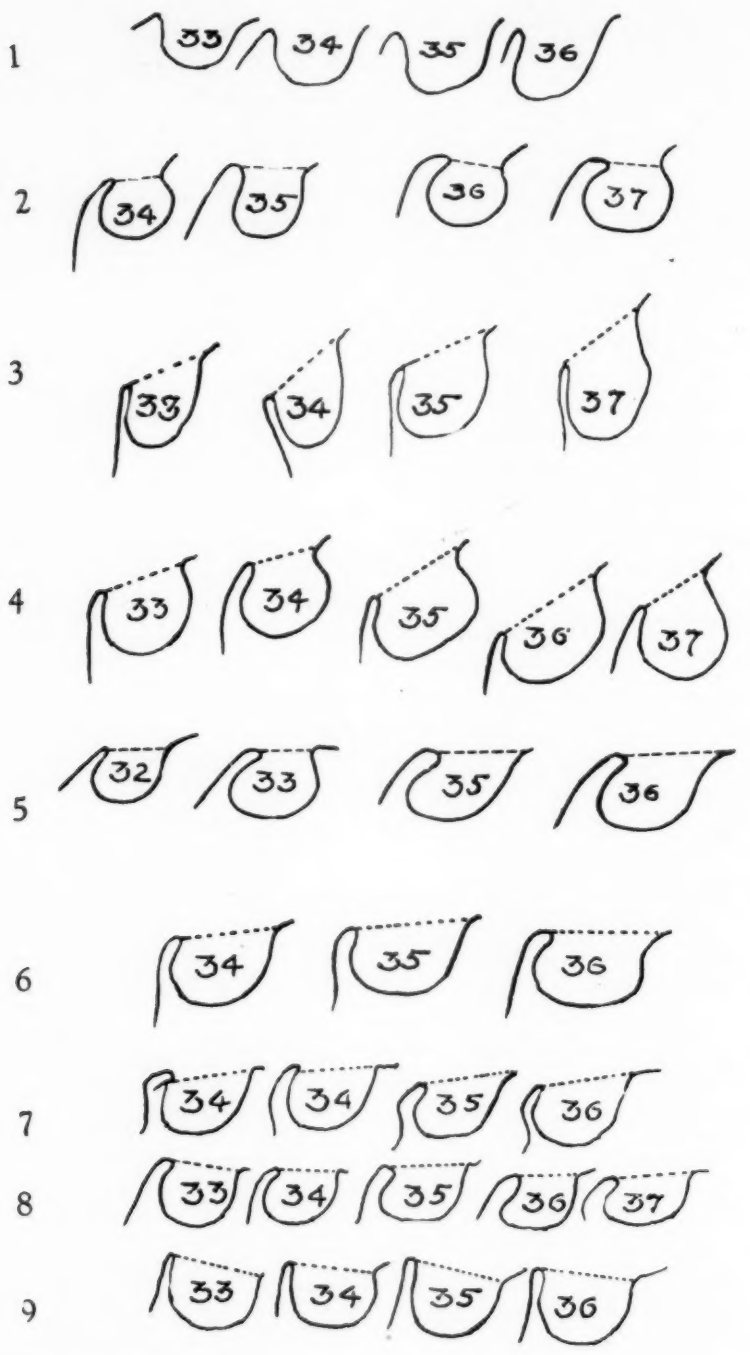

FIG. 2. Outlines of sella turcicas as in Figure 1.

1. Median type: T. R., male, Am. Negro. 1933, 51.6 sq. mm.; 1934, 67.7 sq. mm.; 1935, 80.6 sq. mm.; 1936, 94.2 sq. mm.

2. Round type: R. M., male. 1934, 59.3 sq. mm.; 1935, 69.7 sq. mm.; 1936, 80.6 sq. mm.; 1937, 83.9 sq. mm.

3. Expanding type: L. D., female, Am. Negro. 1933, 79.2 sq. mm.; 1934, 93.4 sq. mm.; 1935, 103.2 sq. mm.; 1937, 129.0 sq. mm.

4. Changeable type: M. S., female, Italian. 1933, 105.8 sq. mm.; 1934, 110.9 sq. mm.; 1935, 114.8 sq. mm.; 1936, 118.7 sq. mm.; 1937, 126.4 sq. mm. (*Legend concluded on next page.*)

in sella size show the largest correlation of any combination.

One other possibility was investigated. The increase of the area of the sella turcica may be merely correlated with increase in area of the sagittal section of the brain cavity, or its modulus length×height. So the correlation was computed between the ratio:

$$\frac{\text{area of sella turcica}}{\text{area of sagittal section of brain case}}$$

on the one hand, and body weight on the other. This was found for males to be $r=0.617\mp0.160$. This is a fairly high correlation and leads to the conclusion: Per unit of cranial sagittal section, the area of the sella turcica is significantly correlated with body weight.

Since mean body weight increases with mean age during adolescence and the size of the head does also, and since sella size is correlated with that of the head, a partial correlation was computed between area of sella and body weight holding area of the cranium ($L\times H$) constant. This correlation was computed on 15 LVD_{II} boys fourteen to eighteen years of age. The result was $r=0.39\pm0.22$. This correlation is hardly significant and so one must conclude that such correlation as there is between size of cross-section of sella and body weight depends chiefly on the increasing size of the head.

CONCLUSIONS AND SUMMARY

The area of the sagittal section of the sella turcica varies with age between ten and eighteen years, usually increasing with age, but in some individuals apparently decreasing, at least for a time. It varies with sex. Thus with children of fifteen years the mean for 23 boys is 81.09 ∓ 4.02 sq. mm., for 34 girls it is 92.94 ∓ 4.07 sq. mm. It makes about the same annual increase in both sexes between twelve and eighteen years; so the sex difference is established early. There is probably a real though slight correlation between area of sella and body weight but the amount of increase in sella area in any period and increase of weight in that period are not significantly correlated; though sella area in relation to brain case area is fairly strongly correlated with body weight at the same time.

2. DEVELOPMENT OF THE FRONTAL SINUS

a. General. It has been shown that in individuals the head length often undergoes an increase in speed of growth in boys at between fourteen and sixteen years of age. This is, indeed, the period of the adolescent spurt of growth, and the increase in speed may be considered in part a special manifestation of a more general growth phenomenon. However, at this time other changes in the cranium occur that affect its length and are of special importance in the development of the glabellar region, usually in association with the frontal sinus. Davis[2] has given the averages of sinus size in an extensive series of skulls from eight days to twenty-five years (unfortunately not sexed). This table shows that vertical and anteroposterior diameters of the frontal sinus undergo a maximum increase at about fourteen years, but the number of skulls at each year of age is small—1 to 4 in the post-juvenile period.

In our studies we have had the very great advantage of consulting a series of roentgenograms taken laterally, and repeated at yearly intervals upon each child. These roentgenograms were taken by one of us (O. R.). The technique was the same as described at the beginning of the article.

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5. Rapidly increasing type: C. M., female. 1932, 50.3 sq. mm.; 1933, 88.3 sq. mm.; 1935, 96.8 sq. mm.; 1936, 111.6 sq. mm.

6. Rapidly growing type: H. S., female. 1934, 104.5 sq. mm.; 1935, 116.8 sq. mm.; 1936, 123.8 sq. mm.

7–9. One fraternity: *8* and *9* Gar. twins, Italian, female. *7*, J. G., male. 1933, 86.9 sq. mm.; 1934, 77.4 sq. mm.; 1935, 83.9 sq. mm.; 1936, 83.9 sq. mm. *8*, A. G. (No. 1) 1934, 74.2 sq. mm.; 1935, 71.0 sq. mm.; 1936; 77.4 sq. mm. *9*, M. G. (No. 2) 1933, 72.1 sq. mm.; 1934, 52.8 sq. mm.; 1935, 67.6 sq. mm.; 1936, 58.1 sq. mm.

b. Method. The method employed by us of making comparisons of the roentgenograms in successive years for changes in the frontal sinus was to place the film on a plate of ground glass illuminated artificially below and to trace on tracing cloth the outline of the inner and outer limits of the cranium as seen in sagittal section. The outlines of successive years were superimposed. In such superposition the matter of appropriate centering arose. The sella turcica, as a well-defined body in the base of the cranium, was taken as a center and the orbital plate of the frontal bone as the radius of orientation. In some cases the outlines of the cranium were used for reference.

c. Growth of the Frontal Sinus. Figure 3 shows the results of such superposition. These are outlines of the cranium of L. C., male, born in October, 1921. The roentgenograms were made on his birth month when eleven (1932), thirteen and fifteen years old respectively.

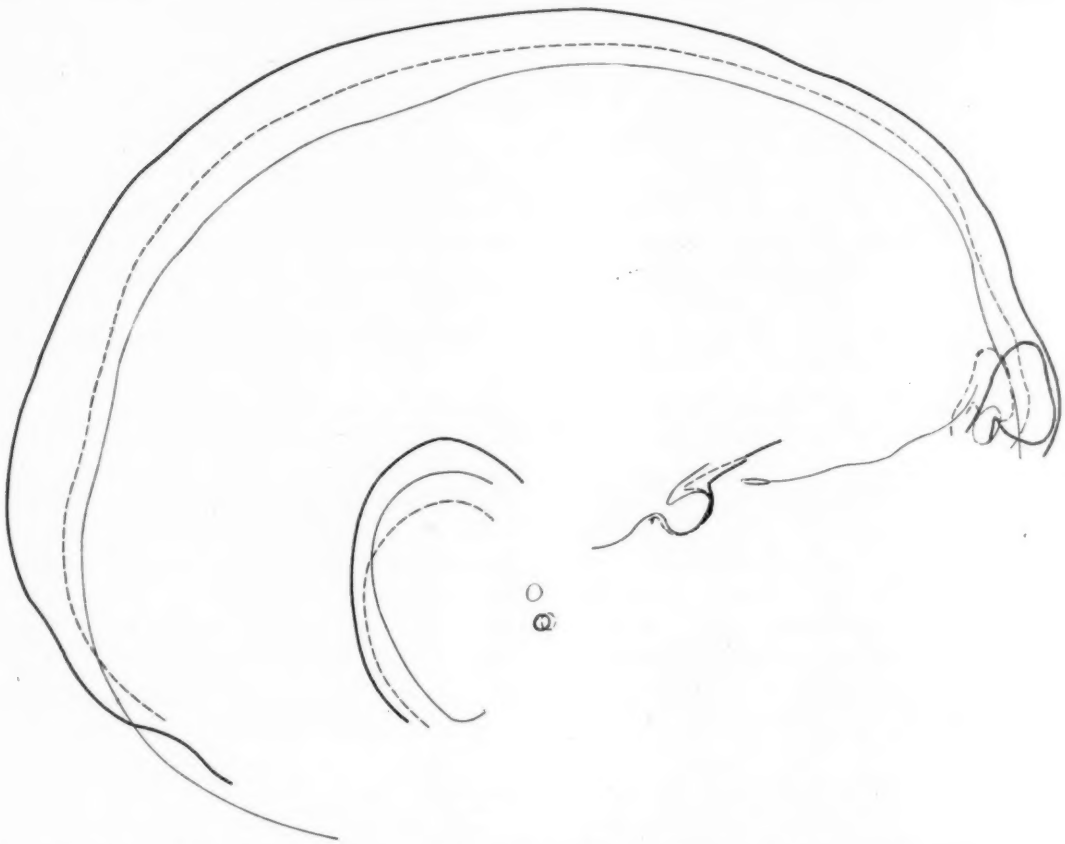

FIG. 3. Sagittal optical sections (from roentgenograms) of head of L. C., male, No. 22, born 1919, in 1932 ———; 1934– – – –; 1936———. These sections are superimposed using the sella turcica as a center and making the contours of cranium approximately parallel. The following points are shown in the figure: Changes in size and form of frontal sinus whose cross-sectional area in the successive years is 45.2, 132.2 and 270.9 sq. mm. respectively. The external auditory meatus migrates downward. The 1936 contour at base of skull seems to be above that of 1932—thus the vertical diameter of the cranium is not increasing. The outlines of the pinna in successive years are drawn in.

Several things appear from a study of Figure 3. First, the skull cap increases in size both anteriorly, dorsally and posteriorly; more posteriorly than in the other radii. Ventrally, the outlines of the later years are *inside* that of the earliest suggesting a flattening of the occipital bone around the foramen magnum or occipital condyles.

Second, the external auditory meatus

varies in position in a way that suggests a differential growth along the axes of this part of the temporal bone.

Third, the frontal region, in the vicinity of the glabella, shows the frontal sinus at the three periods. In 1932 it is a small cavity, about the size of a pea; two years later it had increased, partly by a thickening of the frontal bone on the inner side; in 1936 it had doubled in size and the contour of the forehead now bulged forward. The outer table of the bone has become very thin.

This method of representing the growth of the cranium as a whole leads to a confusion of outlines. For the study of changes in outline of one organ it is necessary to superimpose the outlines of that organ separately, centered at some convenient point.

Figure 4 is the sagittal section of the head of an Italian boy, J. D., born in June, 1923. The outlines were taken on his birth month in 1932, 1934, 1936 and 1937. The superimposed outlines are centered at the sella and the main cranial contours made parallel. A slight flattening occurs at the foramen magnum. The position of the porion is shifted markedly. The frontal sinus enlarges and the frontal bone is thickened on its cerebral border.

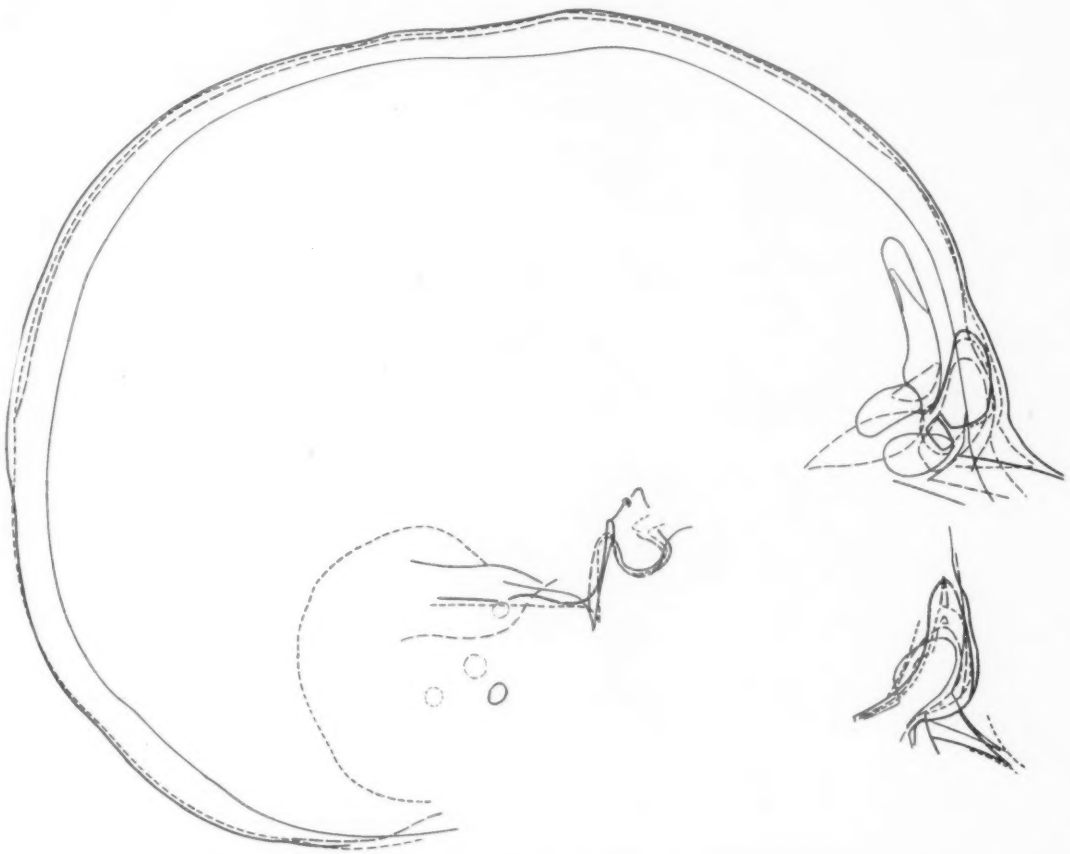

Fig. 4. Sagittal optical sections (from roentgenograms) of head of J. D., male, No. 30, born 1923, in 1932 ———; 1934 – – – – 1936—— and 1937———. Sections superimposed as in Figure 1. The following points are shown in the figure: (1) The frontal sinus with its changes in form in successive years (also given as inset). Areas in successive years are: 1932, 138.6 sq. mm.; 1934, 177.4 sq. mm.; 1936, 203.1 sq. mm. and 1937, 296.7 sq. mm. (2) Migration of external auditory meatus. (3) Meeting of head outlines at base of skull—small growth of vertical diameters.

On Figures 5, 6 and lower right hand corner of Figure 4 are given 13 series of roentgenographic sagittal sections of frontal si-

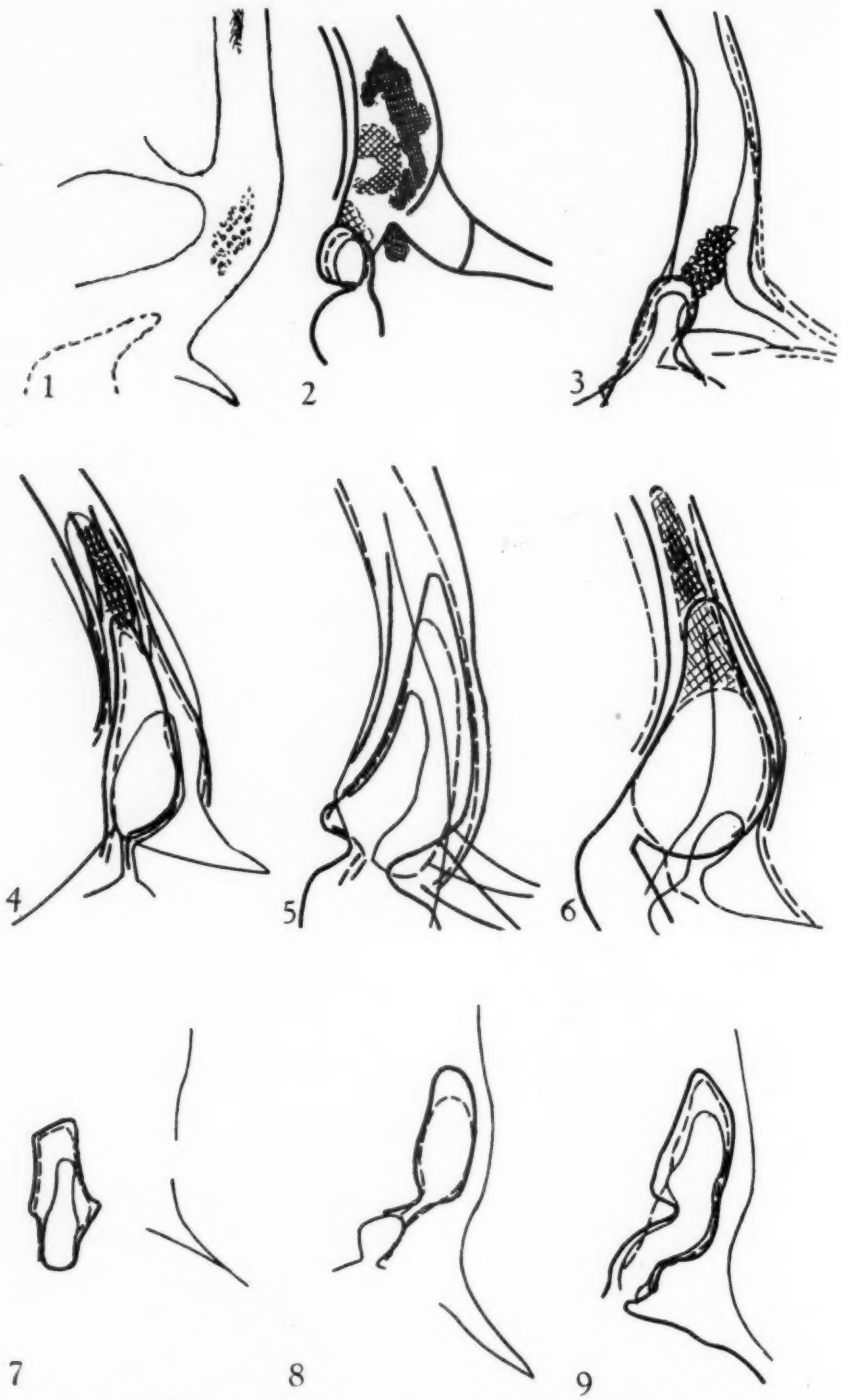

Fig. 5. *1.* Frontal sinus (undeveloped) of M. W., female, ateliotic dwarf at age of twenty-three.

2. Development of cross-section of frontal sinus of J. M., male, No. 73, born 1920. Outlines superimposed in 1934———; 1936------; 1937———. Area at 1937, 21.3 sq. mm.

3. Development of cross-section of frontal sinus of E. C., female, No. 25, born 1919. Outlines superimposed. 1933———; 1934-------; 1935———. Areas at 1933, 32.3 sq. mm.; 1934, 38.1 sq. mm.; 1935. 64.5 sq. mm.

4. Development of cross-section of frontal sinus of S. K., female, No. 123, born 1920. Outlines superimposed. 1932———; area 121.3 sq. mm. 1934------; area 161.3 sq. mm. 1937———; area 200.0 sq. mm.

(*Legend concluded on next page.*)

nuses taken repeatedly on the 13 children.

In Figure 5 (*1*) shows a case of absence of frontal sinus in an ateliotic dwarf girl. Only a small area of spongy bone appears and the frontal bone is quite thin. In (*2*) the sinus is exceedingly small and is growing very slowly at fourteen to seventeen years. The spongiosa is fairly abundant and the frontal bone is thickening. (*3*) shows a larger sinus, also growing slowly and with little spongiosa. (*4*) is from a girl. The sinus is enlarging fairly rapidly and the frontal bone is thickening. The ostium remains small. The spongiosa becomes opened up in advance of the enlarging sinus. (*5*) is also from a girl. The sinus is growing rapidly and the growth is accompanied by a marked thickening of the frontal bone mostly on its cerebral portion. The ostium is large. (*6*) is from a boy of ten to fifteen years. The section of the sinus attains a great size and there is a marked protrusion of the frontal bone in the glabellar region. The spongiosa is preparing the way for further advance of the sinus. (*7*), (*8*) and (*9*) are from the Gar. fraternity. (*7*) is the brother whose sella turcica is small and growing slowly. (*8*) and (*9*) are his twin sisters. In (*8*), twin No. 1, the sinus is of submedian size but growing fairly rapidly. In (*9*), twin No. 2, the section of the sinus is twice as large as in her sister and the frontal bone is thicker; which is partly responsible for her greater head length.

In Figure 6 is given an analytical study of the development of the frontal sinus in cross-section of 3 children. (*1*) sections of a boy taken at eleven, twelve and fifteen years respectively. The frontal bone is clearly increasing in diameter. The radius of curvature of the outer surface remains about constant while that of the inner surface diminishes from 75 mm. to 28, to 10 mm. This indicates that the inner face is becoming more sharply concave toward the brain. The thickening of the bone is chiefly toward the interior of the skull. In (*2*) also of a boy at fifteen, sixteen and eighteen years, respectively, the radii of curvature of both inner and outer surfaces of the frontal bone decrease with age. In this case the thickening of the frontal is both inward and outward. (*3*) The third series is of an American Negro boy at thirteen, fifteen, sixteen and seventeen years, respectively. In this case it is clear that the frontal bone is built up on the outer side more than on the inner. The large sinus is penetrated by bony rods.

To give some idea of the variation in speed of growth of the sagittal section of the frontal sinus in different children Table v is presented. We see that in these 5 boys the area ranges at last observation from 21 to 690 sq. mm., in the 5 girls from 64 to 364 sq. mm. The smallest area is from an eighteen year old girl and the largest from a fifteen year old girl. The range in size is greater in the boys. The largest increment given in the table is 136 sq. mm. during two years. The smallest is 2.1 sq. mm. during two years.

The rate of increase of the area of the section of the sinus is not constant through the years. Thus in the case of Nicholas Dom. the area increased 68 sq. mm. in the course of three years and then, at age fifteen to sixteen, 290 sq. mm. in a single year. Carl Jac.'s sinus increased 136 sq. mm. during

5. Development of cross-section of frontal sinus of E. A., female, No. 124, born 1922. Outlines superimposed. 1932———; area 114.8 sq. mm. 1935-------; area 296.1 sq. mm. 1937———; area 364.4 sq. mm.

6. Development of cross-section of frontal sinus of C. J., male, No. 53, born 1921. Outlines superimposed. 1931———; area 34.2 sq. mm. 1933-------; area 306.3 sq. mm. 1936———; area 425.7 sq. mm.

7. Development of cross-section of frontal sinus of J. G., male, No. 114, born 1919. Outlines superimposed. 1934———; area 41.9 sq. mm. 1935-------; area 96.8 sq. mm. 1936———; area 116.1 sq. mm.

8. Development of cross-section of frontal sinus of A. G., sister of above, No. 44, born 1921. Outlines superimposed. 1934———; area 27.7 sq. mm. 1936-------; area 61.2 sq. mm. 1937———; area 104.5 sq. mm.

9. Development of cross-section of frontal sinus of M. G., twin of above, No. 45, born 1921. Outlines superimposed. 1934———; area 141.9 sq. mm. 1936-------; area 194.1 sq. mm. 1937———; area 225.8 sq. mm.

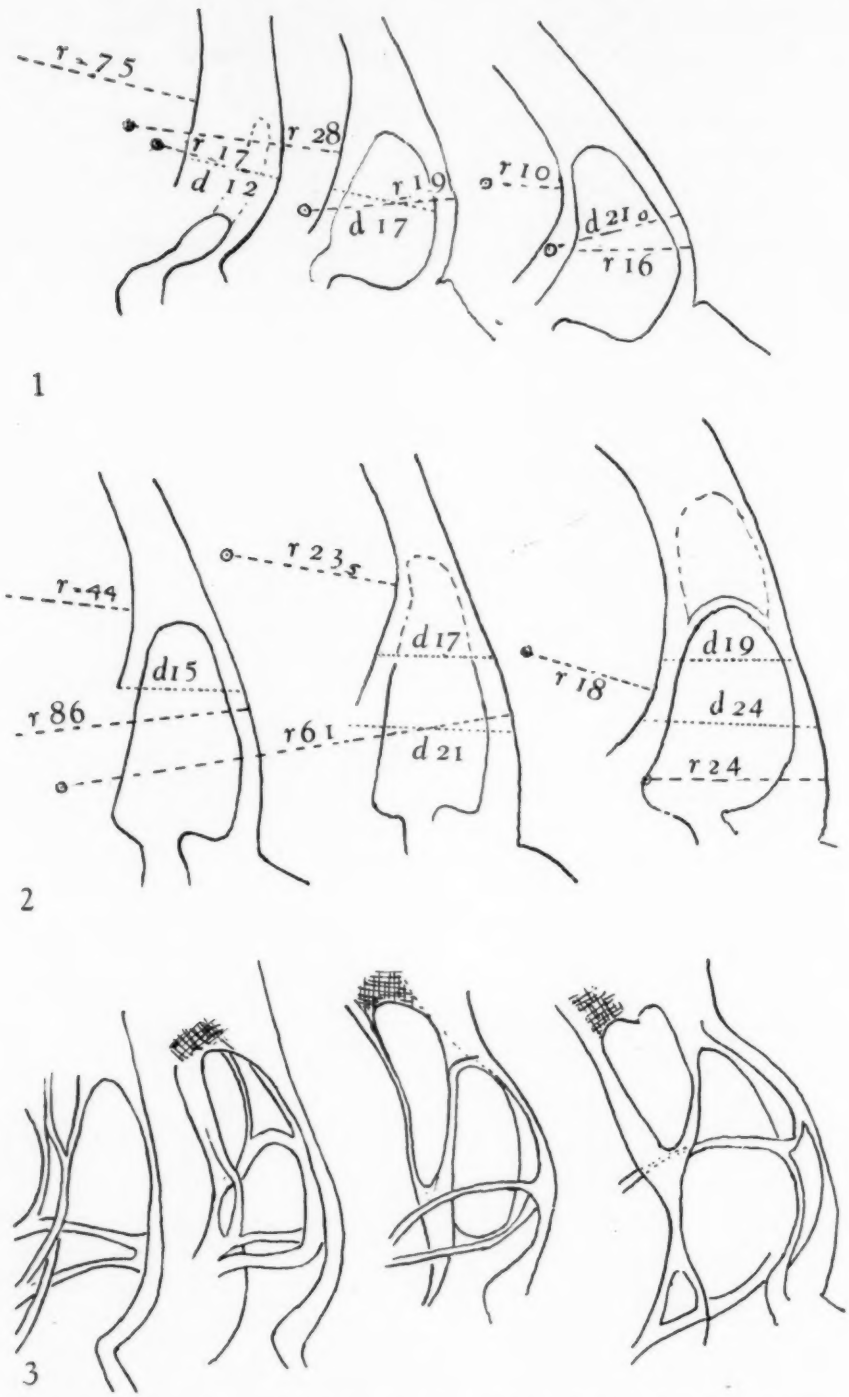

FIG. 6. *1.* Three stages in development of sagittal section of frontal sinus of C. J., male, No. 53, born 1921 (see also Fig. 5, *6*). Taken in 1931, 1933 and 1936, left to right respectively. Diameters of frontal bone (*d*) and radii of curvatures (*r*) of inner and outer face of the bone are indicated.

2. Three stages in development of sagittal section of frontal sinus of N. D., male, No. 34, born 1919. Taken in years 1934, 1935 and 1937, left to right respectively.

3. Four stages in development of sagittal section of frontal sinus of T. R., male, No. 91, Am. Negro, born 1919. Taken in years 1932, 1934, 1935, 1936, left to right respectively. Shows bony struts and plates penetrating the sinus. Impossible to measure area of cross-section accurately.

two years and then only 40 sq. mm. during three years. What causes the variation in size of the sinus at a given age or the speed of its enlargement is quite unknown.

d. The Process of Pneumatization. The series of roentgenograms taken repeatedly on the same individual at yearly intervals give vivid pictures of the process of enlargement of the frontal sinus—a process known as pneumatization.

Table V

VARIATION IN SIZE AND SPEED OF ENLARGEMENT OF MEDIAN SAGITTAL OPTICAL SECTIONS OF THE FRONTAL SINUS IN 12 CHILDREN

Name	Birth Year	Increase in Area in sq. mm.			Area in sq. mm. at Last Observation	Age at Last Observation
		Boys				
John McQ.	1920	6.0 (2)*	6.0 (2)		21.3	17
Joseph Gar.	1919	54.9 (1)	19.3 (1)		116.1	17
Leonard Cal.	1919	43.5 (2)	69.4 (2)		270.9	17
John D'Ami.	1923	19.3 (2)	12.9 (2)	93.5 (1)	296.7	14
Carl Jac.	1921	136.1 (2)	39.8 (3)		425.7	15
Nicholas Dom.	1920	61.0 (1)	67.8 (3)	290.2 (1)	690.0	16
		Girls				
Emily Car.	1919	12.9 (2)	2.1 (2)		64.5	18
Sophia Kon.	1923	20.0 (2)	12.9 (2)		200.0	14
Angelina Gar.	1921	16.8 (2)	43.3 (1)		104.5	16
Mary Gar.	1921	26.1 (2)	31.7 (1)		225.8	16
Edna Abb.	1922	60.6 (3)	33.9 (2)		364.4	15
Clara Eng.	1920	64.5 (2)	35.5 (2)		296.7	17

* Numbers in parenthesis indicate the interval in years during which the increase took place.

The ground for the development of a frontal sinus is, as it were, laid first by the very structure of the frontal bone as seen in cross-section. In this bone there is an inner layer and an outer layer called the diploe; and in between them a layer of varying thickness composed of "spongy" bone, which in the dried skull contains "air cells" or air passages whose diameter is 0.5 mm. or more. In the region of the glabella the texture of the spongy layer is especially open. In the living bone the contents of the cells of the honeycomb, or sponge work, comprise cholesterol, as zu Jeddeloh[7] has shown.

The second factor in the formation of the frontal sinus is the presence of an epithelial layer which is adherent to the periosteum that forms the wall of the nasal cavity in the ethmoid region (Maximow and Bloom).[10]

The first obvious changes in the cross-section of the frontal bone, in anticipation of the formation of a sinus, is an enlargement of the "cells" of the honeycomb work. This enlargement may occur at various parts of the frontal bone, but is most active next to the ethmoid region. Of the nature of the enlargement we have little precise knowledge. Within a few months after birth an interaction seems to take place between the nasal epithelium and its periosteal layer, on the one hand, and the bony partitions of the honeycomb work such that the partitions break down, and the "cells" become enlarged in the upper region of the ethmoid cavity as we see in Figure 5 (*3*). It is probable that osteoclasts are at work in this process and perhaps the lipoids provide energy for these operations. The major operations begin at the nasal membrane and are associated with that membrane. Probably the osteoclasts arise, as is usual, from the periosteum. Their efficiency in dissolv-

ing bone is notorious. Into the cavity formed by the flowing together of the enlarging spaces in the diploe the nasal membrane sends out a pocket. This process is continued usually till the extensive, often lobed, sinus is formed. But in some cases the development of a sinus is stopped almost at the outset, as we see in Figure 5 (*1*). Figure 5 (*1*) to (*9*) and those of Figure 6 are optical sagittal sections; the enlargement of the sinus is usually taking place laterally even more extensively than in the sagittal region.

The development of the frontal sinus is a special case of a process that is widespread among the birds, where all the principal bones are pneumaticized.

Just what determines the course of events that lead to the development of a frontal sinus of a given shape and adult size is unknown. Evidence on the question whether the end-results are due merely to heredity is attained by a comparison of the course of development of the sinuses in the carefully studied and by almost all criteria monozygotic Gar. twins. Yet while at fourteen years twin No. 1 had a sinus in cross-section 35×7 mm., twin No. 2 had a sinus in cross-section 13×3 mm., though accompanied by an enlarged spongy interspace to an axial distance of 35 mm. At the same age the brother, J. G., had a sinus of cross-section 9×4 mm. Thus twins with identical inheritance differed strikingly in degree of development of the frontal sinus, so that we may conclude that non-genetical factors influence the development of the frontal sinus.

e. Significance of the Frontal Sinus. A great deal has been written on this subject; much of it from too narrow a point of view. It has been suggested that the sinus is an organ to increase the olfactory surface. In dogs, indeed, there are sense buds on the lining of the sinus and they are reached by the deeply sniffed air; but no such sense buds occur on the human sinus. Weidenreich[13] finds the sinuses to represent, as it were, the voids between the more or less rounded essential organs of the head; but this is not a good explanation of the frontal sinus. Bütschli's[1] theory that sinuses are the result of bone-economy is related to the last; also the theory that sinuses are for the purpose of reducing the weight of the head. The suggestion has also been made that the sinuses increase the respiratory area as in birds; but this interpretation meets the snag that the circulation of the sinuses is very poor.

In seeking an explanation of the frontal sinus we have first the fact of its great variability down to not infrequently entire absence. This suggests that the frontal sinus at least is not very important today; is, indeed, a rudimentary organ. As such it has been derived from a condition in ancestry where it was important. If we consider other mammals we shall find in general that in quadrupeds with heavy skull the sinuses are numerous and large. The huge elephant's skull is, indeed, largely made up of sinuses surrounding great columns of dense bone that make it (with all its light weight) capable of withstanding great shocks. Obviously the weight of the elephant's head would be intolerable to carry were it composed of solid bone. Man inherits the same tendency to keep down head weight, even though, because his head is balanced on the spine, the weight reduction is less essential. This tendency is still shown, though the variations have little selective value. The maxillary sinus probably has more selective value since it influences more the form of the face.

It might be urged that the frontal sinus by controlling the form of the superciliary, or supraorbital arches, gives the male a virile appearance that has a selective value. This assumes that there is a necessary relation between size of these arches and size of the frontal sinus. As Schaafhausen and others assert it has been repeatedly pointed out that this relation is not close since large supraorbital arches may contain only an exceptionally thick spongy layer and no true sinus.*

* A striking case of the sort is to be seen in the Daniel Baugh Institute of Anatomy of Jefferson Medical College, Philadelphia, Dr. J. Parsons Schaeffer, Director.

On the other hand, large (deep) nasal sinuses cannot be in thin or shallow frontal bone. The thickening, however, may be on the inside so that the torus is not enlarged (Fig. 6, *1*) but more frequently the arches bulge out as the sinus enlarges (Fig. 6, *2*, *3*). So we may conclude that large supraorbital or superciliary arches are not always evidence of large frontal sinuses; but that large frontal sinuses imply a thickening of the spongiosa in the skull which may give rise to either internal or external bulging, and more commonly the latter.

SUMMARY

A series of roentgenograms taken at different ages on the same individuals shows that the frontal sinus begins by a destruction of the spongy layer of the frontal bone above the ethmoid. Into the space thus formed the nasal epithelium outpockets. The sinus thus initiated enlarges as the osteoclastic process continues. At the same time the frontal bone in this region thickens and the outbulging may affect chiefly the inner face, or the outer face, or both faces of the frontal bone. The degree of development of the sinus is varied at adolescence from 0 to 700 sq. mm. in cross-section at the glabella. The development of the frontal sinus is a special case of pneumatization. It is probably a rudimentary process, being relatively unimportant for man in whom the skull is balanced on the vertebral column.

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THE USE OF THORIUM DIOXIDE IN ROENTGENOGRAPHY OF THE SINUSES*

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IN THE diagnosis of infection of the paranasal sinuses roentgenograms are invaluable. This is especially true in those cases which show no evidence in the nose of involvement of the sinuses such as pus or polyps and in which the sinuses are normally translucent. There are certain conditions such as asthma, arthritis, nephritis, bronchitis, bronchiectasis, uveitis, chorioretinitis, colds and headaches that are regarded as dependent on some focus of infection. When one is searching for a focus in such conditions, apparently normal sinuses should be roentgenographed. The plain roentgenograms may definitely indicate sinus infection, they may show only slight changes in the sinus membranes, or they may be clear. Since slight changes may be found in healthy individuals, those patients suspected of harboring a focus of infection should be further examined to determine if there is definite pathologic change in the sinuses and, if so, if there is enough to justify surgical treatment.

It has been customary in such cases to inject iodized poppy seed oil (40 per cent) into the sinus cavities or utilize the displacement method of Proetz. The iodized oil being opaque outlines the membranous wall of the sinus and thus records the thickness of the membranes and may show the presence of polyps, cysts, or tumors of the antrum. But because it is so opaque it often obscures even sizable polyps or cysts if they are in such position as to cause little defect in the marginal outlines of the sinuses.

It was not until the spring of 1938 that we discovered in a rather indirect way what we feel is a better method of bringing out changes in the sinus membranes by roentgenography after injecting an opaque medium. A patient in our Allergy Clinic with an idiosyncrasy to iodine had severe bronchial asthma. The roentgenograms of the sinuses showed a moderate thickness of the antral membranes. Since the general condition was not good, operative procedures were not indicated without conclusive evidence of extensive pathologic change. After consultation with Dr. William H. Boone of the Department of Roentgenology and Dr. Simon A. Beisler of the Department of Urology, it was decided to try a colloidal solution of thorium dioxide† since the patient's sensitization precluded the use of any iodine preparation. Using this contrast medium to which there was no sensitization, sufficient changes were demonstrated to justify an operation. We were impressed with the delicacy, if one may call it such, of the shadows. The solution seemed to produce a less dense shadow and the margins and backgrounds were more clearly delineated. Since that time we have injected 117 patients,‡ 17 of whom have been operated upon and the pathological condition confirmed. Four of our cases with reproductions of the roentgenograms of one will be described in more detail later.

Umbrathor is a colloidal solution containing 25 per cent thorium dioxide. It is a stable, brownish liquid, transparent in transmitted light and of milky appearance in reflected light. After storage over a long period of time a small amount of sediment may appear which is not objectionable as it is resuspended upon shaking. It is adjusted to a pH of 2.8. It should be stored in a temperature of 60° to 70° F. No harmful effects from secondary rays have been ascer-

† We have used the commercial preparation, umbrathor, manufactured by Heyden Chemical Corp., New York.

‡ Dr. John G. Welch and Dr. Albert W. Dodd, Jr., assisted in the injection of the umbrathor.

* From the Departments of Allergy and Otolaryngology, Roosevelt Hospital, New York. Presented before the New York Academy of Medicine, Section of Otolaryngology, Dec. 20, 1939.

tained. It is not absorbed, and it is claimed to be non-toxic and non-irritating.

The adaptability of this solution for visualization of mucosae by roentgenography is based on the fact that the preparation is flocculated as a surface coating. Naturally, therefore, such mucosae as those of the stomach, intestines and bladder which have rugae are strikingly visualized. We have found that pathologic changes in sinus membranes are more evident on the film after antral injection with thorium dioxide than they are with the plain film or after the use of iodized oil.

Various solutions of thorium compounds have been used for visualization of body cavities by roentgenography. Burns[1] in 1915 used a solution of double citrate of sodium and thorium, together with an excess of sodium citrate and some sodium nitrate for making pyelograms. Kalkbrenner[2] in 1928 used a colloidal solution of thorium dioxide for bringing out the details of the intestinal mucosa in roentgenograms. In 1932 Ritter and Rattner[3] presented a study of the use of umbrathor in urography. Thorotrast, a 25 per cent solution of thorium dioxide, has been used by intravenous injection for hepatolienography and peripheral cerebral arteriography.

In selecting a solution for a contrast medium in roentgenography it must in the first place be opaque to the roentgen ray. Since the opacity is in direct proportion to its atomic weight, thorium, being next to the heaviest known element, should be an ideal medium. There are several other requisites. The contrast medium should be non-toxic and non-irritating, it should give a good shadow as well as a clear delineation, it should have such fluidity as to render injection easy. It is further desirable that it should be inexpensive and should not stain. Since the 25 per cent colloidal solution of thorium dioxide may be diluted with one to two parts of distilled water it is inexpensive and in our experience fulfills all the other requisites mentioned.

The technique of the injection is the same as that used in irrigating the sinuses. Ten to 20 cc. of the diluted umbrathor is introduced into the antrum through a Coakley trocar or an 18 gauge spinal puncture needle after cocainization. The sphenoidal or frontal sinuses may be injected with the proper cannulae. The solution may be left in the sinus or after five or ten minutes drawn off or removed by the insufflation of air. We have taken the roentgenograms from fifteen to forty-five minutes after the injection. Several cases from which the excess solution was not withdrawn or expressed by insufflation were roentgenographed again twenty-four and forty-eight hours later and some of the opaque medium was shown to be still present. In most cases the sinuses were irrigated the next day to remove any of the remaining solution. One case in which some of the solution was injected into polypoid tissue when the needle punctured it showed an opacity when roentgenographed six months later, but apparently no symptoms were being caused by its presence.

We have found the injection of a colloidal solution of thorium dioxide as an opaque contrast medium particularly useful in diagnosing pathologic conditions of the sinuses in our allergic cases. The pathologic change in the antra of these cases is frequently a cystic degeneration or an edematous one. Plain roentgenograms often do not delineate these changes clearly. Another type of case which is suited to the injection of this medium is one which transilluminates poorly although the ordinary roentgenograms look clear. We have demonstrated mucous polyps in the antra of several such cases after an injection of thorium dioxide. A brief description of 4 cases with a reproduction of the roentgenograms of one is herewith presented.

REPORT OF CASES

Case 1. F. H., aged twenty-five, complained of asthma and sneezing. Skin tests showed a sensitivity to house dust. The frontal sinuses and left antrum transilluminated clearly; the right antrum was cloudy. There was evidence of discharge from the right antrum. Irrigation of this antrum returned a clump of mucopus.

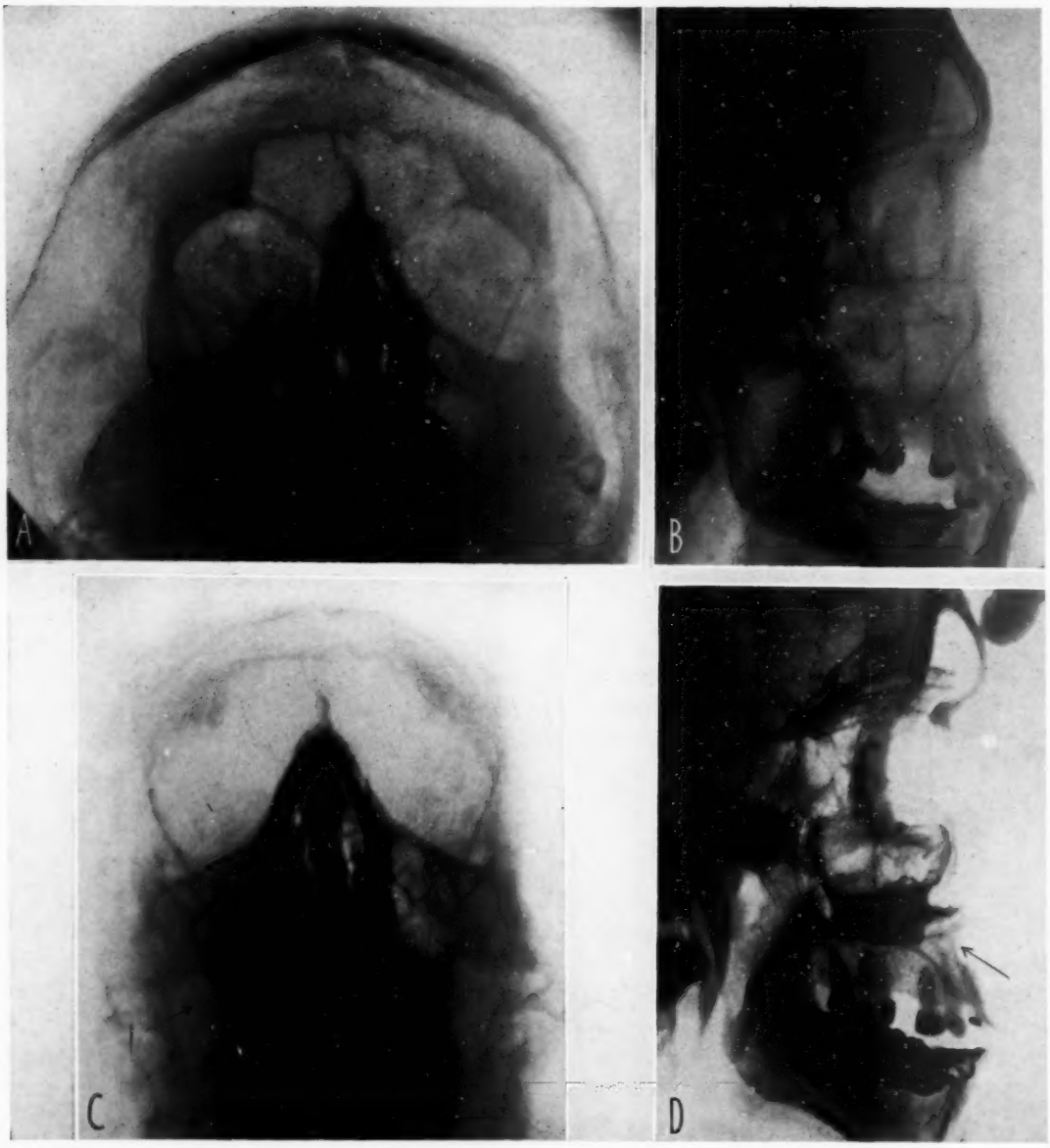

FIG. 1. Case 1. *A*, plain anteroposterior and *B*, lateral roentgenograms of the sinuses. *C* and *D*, roentgenograms made after the injection of umbrathor into the antrum. The arrow indicates the space occupied by the umbrathor.

Plain roentgenograms (Fig. 1, *A* and *B*) showed no pathologic change in the sinus but roentgenograms made after the injection of umbrathor (Fig. 1, *C* and *D*) into the right antrum showed a large filling defect. A Caldwell-Luc operation was performed and much thickened membrane and several large mucous polyps were removed.

CASE II. V. Y., aged fifty-nine, complained of hay fever and asthma. Skin tests revealed a sensitivity to house dust, ragweed and timothy pollens. The frontal sinuses and antra transilluminated clearly. There was a small polyp in the right ethmoidal region which was removed. Plain roentgenograms showed a slight thickening of the membranes of the antra. Irrigation of the right antrum was clear. An injection of umbrathor into the right antrum revealed a large defect apparently from a polyp. A Caldwell-Luc operation was performed and considerable polypoid membrane was found covering the roof and nasal wall of the antrum.

Case III. H. M., aged thirty-two, complained of asthma. Skin tests showed no sensitivity. The frontal sinuses and right antrum transilluminated clearly but the left antrum was cloudy. Nasal examination was negative for pus or polyps. Plain roentgenograms showed a questionable thickness of the left antrum membrane. Irrigation of the left antrum was clear. Umbrathor injection of the left antrum revealed a large defect. This was also confirmed with roentgenograms made after the injection of iodized poppy seed oil (40 per cent). A Caldwell-Luc operation was performed and the membrane was found to be much thickened with many mucous polyps present, several of which were abscessed.

Case IV. L. D., aged forty-five, complained of asthma for seven years. Skin tests revealed a sensitivity to house dust and ragweed pollen. The frontal sinuses illuminated clearly but the antra were dark. The right middle turbinate was enlarged. There was no evidence of pus or polyps in the nose. Plain roentgenograms showed slight clouding of the right antrum. Roentgenograms made after the injection of umbrathor into the right antrum showed large defects in the posterior area and on the floor. A Caldwell-Luc operation was performed on the right antrum and the defects were found to be due to cystic polypoid membrane.

SUMMARY

When looking for a focus of infection in the sinuses it is difficult without roentgenograms to make a diagnosis if the sinus transilluminates clearly and there is no evidence of pus or polyps in the nose. The plain roentgenograms are not infallible and in such cases it is advisable to inject a radiopaque medium into the sinuses and make new roentgenograms. Because of the not infrequent idiosyncrasy to iodine in allergic patients and because iodized oil often obscures polyps and cysts by the density of the shadow, we have resorted to the use of a dilution of 25 per cent colloidal solution of thorium dioxide. This gives a very clear delineation of polypoid degeneration of the sinus membrane, even when diluted with one or two parts of distilled water. The sinuses of 117 patients have been injected with this solution without any untoward reactions. Four illustrative cases are described in which roentgenograms after the antral injection of thorium dioxide were very important in establishing the diagnosis of hyperplastic sinusitis.

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ACUTE MEDIASTINITIS*

ROENTGENOLOGICAL, PATHOLOGICAL AND CLINICAL FEATURES AND PRINCIPLES OF OPERATIVE TREATMENT

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IN THIS contribution the subject of acute mediastinitis will be presented with special reference to its roentgenological aspects. Such a presentation is appropriate because the diagnosis and localization of the lesion, and the surgical approach, are all based on information derived largely from roentgenological examination. Indeed, this disease is an outstanding instance in which the clinician must lean heavily on the roentgenologist for diagnosis. In order to appreciate fully the significance of the various roentgenological features that are encountered in cases of acute mediastinitis, some knowledge is necessary of the pathogenesis, pathology, clinical features, and surgical aspects of the disease. These will be presented on the basis of our experiences. No effort will be made at completeness, our chief purpose being to set forth the various features in relationship to the roentgenological aspects of acute mediastinitis.

The presence of contrasting air in the trachea, and the delineation of the mediastinum as a whole by the air in the adjacent lungs, furnish the main anatomical and physiological factors which enable one to differentiate the mediastinal organs roentgenologically. Moreover, the possibility of introduction of radiopaque materials into the esophagus and tracheobronchial tree offers further aid to the roentgenologist in outlining the mediastinal structures. It is thus that the roentgenologic method has been most useful in the study and diagnosis of mediastinal diseases.

Nevertheless, because of the comparative infrequency and inadequate understanding of diseases in this region, and the difficulties attendant upon surgical exploration, together with the reluctance of clinicians to advise operative procedures upon the mediastinum, many of the cases of mediastinal disease remain undiagnosed or untreated. This is true particularly of acute infections of the mediastinum. Acute mediastinitis is decidedly more common than is generally thought to be the case. Thus we have collected 67 cases from the records of Mount Sinai Hospital for a period of ten years, and additional cases were undoubtedly overlooked.

CLASSIFICATION

It will be seen that infections of the mediastinum are of varied etiology and occur in different forms, and that the indication for surgical treatment depends largely upon the etiology and type of infection. Useful classifications of these diseases, therefore, will necessarily take into account both of these factors.

A. Pathological classification
   1. *Mediastinal lymphadenitis*
      a. Non-suppurative
      b. Suppurative
   2. *Phlegmonous mediastinitis*
   3. *Mediastinal abscess*

This classification includes all of the acute mediastinal infections and is essential as a framework for the study of the subject. For the surgical treatment, however, it is also necessary to consider the etiology and pathogenesis of the mediastinal infection.

B. Etiological classification
   1. Post-trauma to esophagus
   2. Post infections of neck
   3. Miscellaneous

Clinically, the division of acute infections of the mediastinum into suppurative and non-suppurative forms cannot always be made with certainty. There are cases in which the clinical and roentgenological fea-

* Readi n part at the Thirty-seventh Annual Meeting, American Roentgen Ray Society, Cleveland, Ohio, Sept. 29–Oct. 2, 1936.

tures may be pathognomonic of non-suppurative mediastinal infection on the one hand, or of mediastinal abscess, on the other. However, there are others in which such differentiation is impossible. On the evidence available in our series of cases, it appears safer to assume in all doubtful cases that suppuration exists.

C. Clinical classification of suppurative lesions
   1. Localized form to which the term "mediastinal abscess" can be attached
   2. Diffuse form best termed "phlegmonous mediastinitis."

Regardless of source or symptoms, mediastinal abscess and phlegmonous mediastinitis are quite different lesions. Although coexisting at times, they should be differentiated whenever possible because there may be a difference in operative indication.

PATHOGENESIS

The two most common causes of acute mediastinitis, which together account for over three-quarters of the cases, are acute infections of the pharynx and injuries to the esophagus.

1. *Mediastinitis Following Infections of the Pharynx.* The pharyngitis which precedes acute mediastinitis is caused by a particularly virulent organism which in our cases was the *Streptococcus haemolyticus B.* The infection extends through the mucous membrane beyond the protective lymphoid tissues into the peripharyngeal connective tissue. Here an abscess may be formed. Whether suppuration takes place in the neck or not, this infection may travel by means of lymphatic channels, producing a more or less evident lymphangitis and perilymphangitis of the tissues in the neck, and descends into the mediastinum. In the cases of simple mediastinal lymphadenitis there may be comparatively little evidence of diffuse infection of the cervical connective tissue, the infection making its way into the lymph nodes of the mediastinum along lymphatic channels.

In mediastinal phlegmon, there is always to be found a corresponding phlegmonous inflammation beginning in the peripharyngeal connective tissue and extending down to the mediastinum. Only rarely is this mediastinal phlegmon associated with suppuration in the connective tissue about the pharynx. In these rare instances, the area of suppuration is small and out of proportion to the size of the cervical phlegmon which overshadows it completely.

A large proportion of the cases of mediastinal abscess occurs by the direct downward extension along the fascial planes of a retropharyngeal or parapharyngeal abscess. In the remainder of the cases of mediastinal abscess following in the course of an acute pharyngitis, the abscess is formed either as a result of the rupture of a suppurative focus in one or more of the lymph nodes (suppurative lymphadenitis) or as the result of localization of the infection in a case of phlegmonous mediastinitis. The last method of production of an abscess of the mediastinum must be rare.

2. *Mediastinitis Following Injuries to the Esophagus.* In the present series, injuries to the esophagus were almost as frequent a cause of acute mediastinitis as infections originating in the pharynx. Almost all of the injuries were perforative. Approximately one-half of them occurred in the course of esophageal instrumentation, such as esophagoscopy, dilatation of strictures, and the implantation of radium seeds for carcinoma. The presence of a carcinoma of the esophagus predisposes to perforation and infection of the mediastinum, which may occur even without instrumentation. Similarly, the action of radium by accelerating the necrosis of the neoplastic tissue may lead to mediastinitis without an actual perforation of the esophageal wall.

Fish bones and chicken bones were the most common perforating foreign bodies in the series. In one instance, perforation followed the ingestion of a meat bone, and on one occasion there was a perforation of a decubitus ulcer caused by the pressure of a toy "jack" which had been lodged in the esophagus for a considerable period of time.

FIG. 1. Para-esophageal abscess following acute pharyngitis and complicated by abscess of upper mediastinum. Lateral view of neck on admission shows only minimal retrotracheal widening.

3. *Miscellaneous Causes of Mediastinitis.* Mediastinitis may come about in other ways. For the most part, single examples of these have come under our observation. An ascending infection of the posterior mediastinum from the retroperitoneal tissues occurred in a case of appendicitis with peritonitis, in which a retroperitoneal phlegmon had been formed. The mediastinum may become involved in the course of general infections. Here there may occur a blood stream metastasis into the mediastinal connective tissue itself, or a secondary involvement of the mediastinum from suppuration in the vertebrae, the wall of the esophagus, or one of the mediastinal lymph nodes. Occasionally in suppurative bronchopneumonia, one of the superficial suppurative foci adjacent and adherent to the mediastinum may rupture into this region and produce a mediastinal abscess. In these cases *Streptococcus haemolyticus B* is usually the offending agent. Similarly, the mediastinum may be invaded by a gangrenous lung abscess which abuts upon the mediastinum.

Perforation of the trachea or main bronchi into the mediastinum occurs very rarely. We have observed acute phlegmonous mediastinitis as a result of perforation of the trachea by a broken down gumma, and as a result of the ulceration of a neoplasm of a main bronchus. In one case, infection of a melanocarcinoma of the mediastinum occurring in a manner which is not entirely clear produced mediastinitis.

PATHOLOGY

In considering the pathogenesis of acute mediastinitis, the etiology is the most important single factor, but from the standpoint of operative treatment the classification of the pathological types mentioned under classification of mediastinitis is of prime importance. It is nevertheless true that a consideration of the rôle of an esophageal perforation in the causation of a mediastinitis is also required for the determination of the indications for operation. The pathological picture of mediastinitis will therefore be considered under three headings mentioned in the original classifi-

FIG. 2. Same case as in Figure 1. Lateral view of chest. The trachea is displaced forward by the abscess in the posterior mediastinum.

cation, and the special pathology of the lesions resulting from esophageal perforation will then be discussed.

1. *Mediastinal Lymphadenitis.* The opportunity to study the pathology of mediastinal lymphadenitis is presented by postmortem examination of patients who have died from related causes, for mediastinal lymphadenitis is not a cause of death.

In the simple form, the lymph nodes are enlarged to a variable degree. They are succulent as a result of an edema which accompanies the inflammatory reaction. Although the capsules of the individual nodes may present some infiltration, there is very little perilymphadenitis. The enlarged lymph nodes are therefore discrete. All of the mediastinal lymph nodes, including the tracheobronchial, may be involved, but those in the median portion of the posterior mediastinum are usually the most inflamed. Often the process extends to the retroperitoneal nodes, which present a picture similar to those of the mediastinum. Enlargement of the lymph nodes of the neck is common and precedes the mediastinal involvement if the infection is primary in the neck.

Fig. 3. Same case as in Figures 1 and 2, two days after admission. Demonstrates rapid increase in size of the retrotracheal shadow.

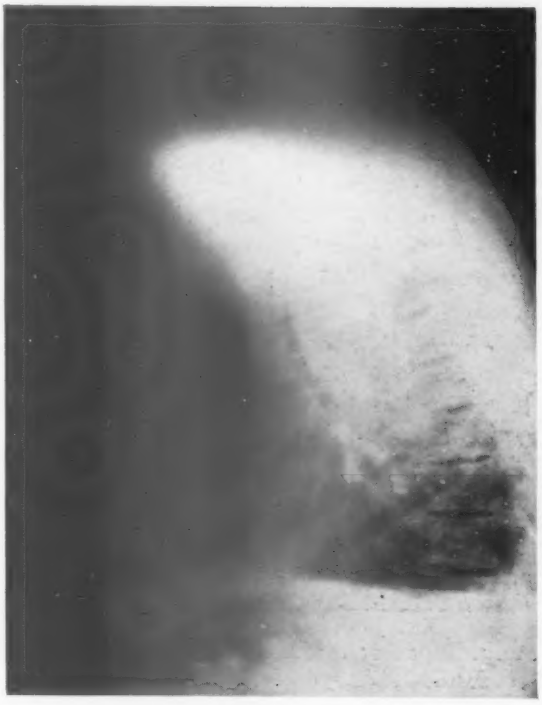

Fig. 4. Same case as in Figures 1, 2, and 3, two days after admission. Further anterior displacement of the thoracic trachea, which now shows anterior bowing.

Suppurative mediastinal lymphadenitis is caused by an infection either of a different character or of greater virulence. Here the lymph nodes are usually larger, are much more firm, and within them are to be found areas of suppuration. The capsule is markedly infiltrated with polymorphonuclear leukocytes, and the inflammatory reaction often extends through the capsule to the connective tissue about the nodes. Here the inflammatory exudate serves to cause the lymph nodes to adhere to one another so that they form a matted mass, but the individual large nodes are still plainly discernible. In unusual instances, perforation of one or more of the suppurating nodes may occur and result in the formation of a mediastinal abscess. Since the entire process is usually secondary to an upper respiratory infection of considerable viru-

Fig. 5. Huge abscess of superior mediastinum complicating acute pharyngitis without cervical suppuration. Recovery followed drainage through posterior mediastinotomy.

lence, there is not infrequently an accompanying bronchopneumonia which represents an infection within the respiratory passages rather than from the lymph nodes themselves within which the infection is fairly well localized.

2. *Phlegmonous Mediastinitis.* Since phlegmonous mediastinitis represents a spreading inflammation of the connective tissue of the mediastinum rather than an inflammation of the lymph nodes themselves, the enlargement of the mediastinal lymph nodes is comparatively insignificant. The structures of the mediastinum are firmly matted together by an exudate which may be of extreme density. All the mediastinal structures are thus imbedded in an indurated inflammatory mass which involves the mediastinum in a diffuse manner. Scattered throughout the inflamed mediastinum are usually seen small, irregular areas of necrosis, some of which may be undergoing purulent softening, but rarely is there present a well defined and localized abscess cavity.

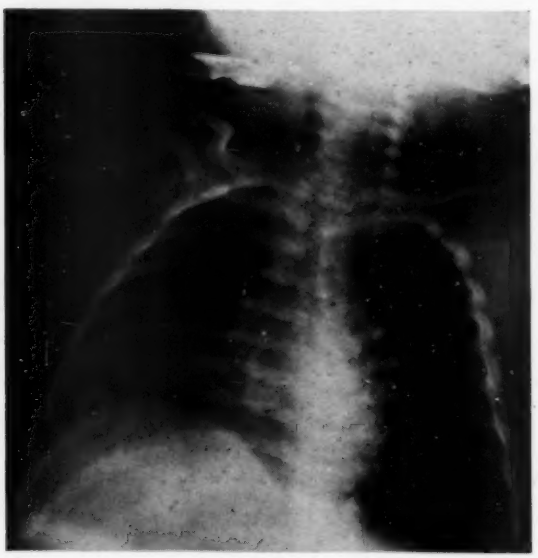

Fig. 6. Abscess of anterior superior mediastinum following acute pharyngitis complicated by paraesophageal abscess. Drainage through the root of the neck was insufficient.

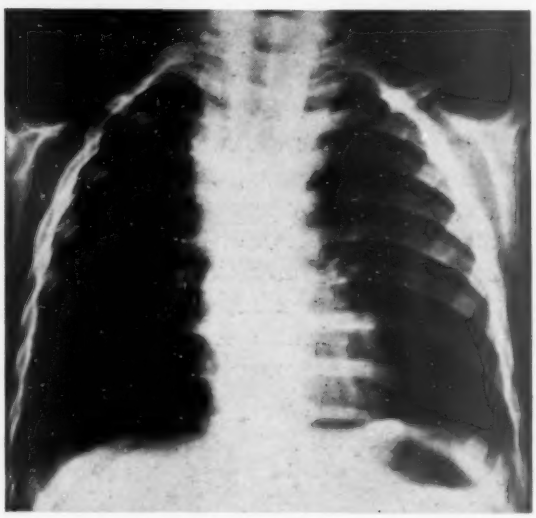

Fig. 7. Abscess of posterior superior mediastinum complicating hypopharyngeal and retro-esophageal abscess. The straight borders suggest the presence of a diffuse phlegmonous mediastinitis. Nevertheless, a high abscess was discovered at necropsy. Phlegmonous mediastinitis occurs rarely in the presence of a cervical abscess.

The tissues of the posterior mediastinum about the esophagus and aorta and in front of the vertebrae are the seat of the most intense inflammation, but the inflammatory

process may extend toward and into the middle and anterior mediastinum.

The parietal pleura covering the mediastinum becomes reddened and soon assumes a granular appearance due to the deposition of fibrin. Within it there can often be seen yellowish streaks representing a purulent lymphangitis of the subpleural lymphatics. This often extends along the root of the lung into the peribronchial connective tissue and the septa of the lungs themselves, eventually reaching the subpleural lymphatics over the surface of the lungs. Here the unusual picture of interlacing strands following the pattern of the subpleural lymphatics may be visible. This is the mechanism of production of lymphangitis of the lung and pleura in cases of phlegmonous mediastinitis. It may soon be complicated by a pleural effusion. Since the spread of the infection occurs simultaneously to both lungs

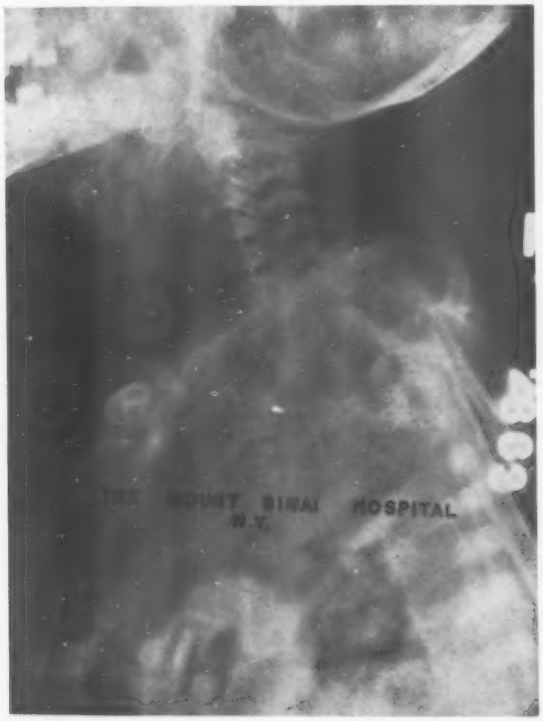

Fig. 8. Same as in Figure 7. The extreme degree of retrotracheal widening indicates the presence of a cervical abscess. Although this was missed on repeated clinical examinations, it was discovered at necropsy.

Fig. 9. Superior mediastinal abscess following perforation of cervical esophagus during esophagoscopy. There is a slight widening of the superior mediastinum with subcutaneous emphysema at the root of the neck.

Fig. 10. Same case as in Figure 9. Lateral view of neck showing marked emphysema of the tissue caused by the air admitted through the large perforation. Recovery following incision of the mediastinal abscess through the neck.

FIG. 11. Superior mediastinal abscess following fish-bone perforation of lower cervical esophagus. Note the widening of the retrotracheal space and the small bubble of air at the site of the esophageal perforation.

from the diffusely inflamed mediastinum, this effusion is usually bilateral. At first the fluid is clear, but soon becomes purulent. The spread of the infection may take place to the pericardium as well as to the pleura. In this way there occurs an acute pericarditis, in association with a bilateral pleuritis in cases of phlegmonous mediastinitis.

The further extension of the infection from the mediastinum along the retroperitoneal lymphatics results in an inflammation of the retroperitoneal tissues which is most marked about the aorta and the prevertebral connective tissue. Here the inflammatory reaction is usually not quite so intense as in the mediastinum itself and it may be localized within the lymph nodes, causing a simple or suppurative retroperitoneal lymphadenitis rather than a diffuse phlegmon. Occasionally the retroperitoneal inflammation extends to the posterior parietal peritoneum and thus produces a sympathetic peritonitis manifested by the exudation of serous fluid into the peritoneal cavity. Later the ascitic fluid may become purulent, and although it may remain sterile for a period of time, eventually the bacteria responsible for the disease—usually *Streptococcus haemolyticus B*—invade the peritoneal cavity.

3. *Mediastinal Abscess.* Because of the great frequency with which mediastinal abscess occurs as a downward extension from a suppurative focus in the neck, the lesion is usually situated in the superior mediastinum. The mediastinal abscess is situated about the esophagus, the smaller ones almost always remaining behind the trachea which is displaced forward to a considerable extent. The upper mediastinal abscesses usually do not extend below the level of the tracheal bifurcation, although in some instances they do burrow downward below this level. The intertracheal lymph nodes may have some influence in confining the abscess above this level. It

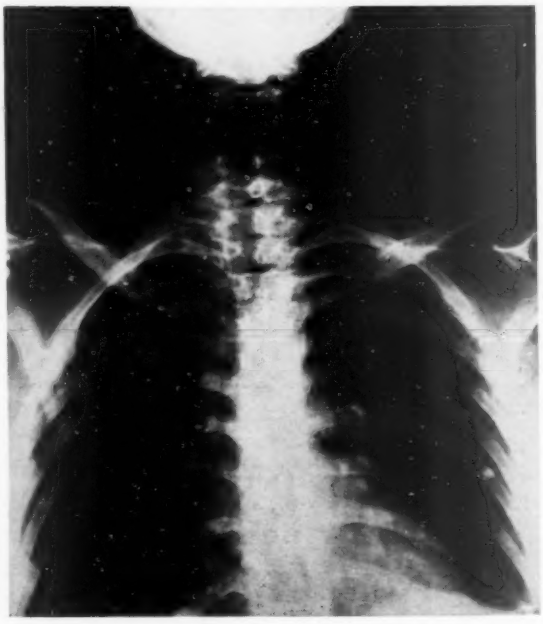

FIG. 12. Abscess at root of neck entering the superior mediastinum following chicken bone perforation of lower cervical esophagus. The bone lies almost transversely at the level of the seventh dorsal vertebra. Patient recovered following the removal of foreign body and drainage of the abscess through the neck.

appears that the aortic arch, as it crosses from right to left from the anterior to the posterior mediastinum, also presents a barrier to the development of the mediastinal abscess in the direction of the left side, for abscesses of the superior mediastinum are usually bounded by this structure and when they enlarge are seen to extend mainly toward the right side. Very rarely does an abscess descend from the neck into the anterior mediastinum. When an anterior mediastinal abscess does occur, it represents an extension from the posterior mediastinum or is due to some unusual cause.

As the abscess grows, the retrotracheal tissues become more and more distended. Occasionally the pus may burrow downward to the level of the diaphragm. The inflammatory process extends to the mediastinal pleura which becomes markedly thickened and may become adherent to the visceral pleura over the mediastinal surface of the lung. Since the abscess has a tendency to burrow toward the right side, adhesions are perhaps more frequent here. The abscess may burrow through the adherent pleura into the right upper lobe and here produce a secondary abscess of the lung. This soon communicates with a posterior bronchus of this lobe (superior paravertebral) through which the contents of the abscess are expectorated. If dense adhesions are not present, the mediastinal abscess may perforate into the free pleural cavity to produce an empyema. Under these circumstances, the mediastinal source may be entirely unrecognized.

Fig. 13. Same case as in Figure 12, showing chicken bone in vertical projection lying in the widened retrotracheal space. Adjacent to it there are a few small bubbles of air from the esophageal perforation.

Fig. 14. Same case as in Figures 12 and 13. Shortly after removal of foreign body and drainage of the abscess.

Abscesses of the lower mediastinum are rare. These of course do not represent a direct downward extension from an abscess of the neck, but are due to a local cause in this region, i.e., perforation of suppurating lymph nodes, esophageal perforation, etc. These abscesses are also situated in the posterior mediastinum. They spread to either side, depending on their point of origin, and may perforate to produce an empyema on the corresponding side.

Modification of Mediastinal Infections in Cases of Esophageal Perforation. With only one exception, the mediastinitis following

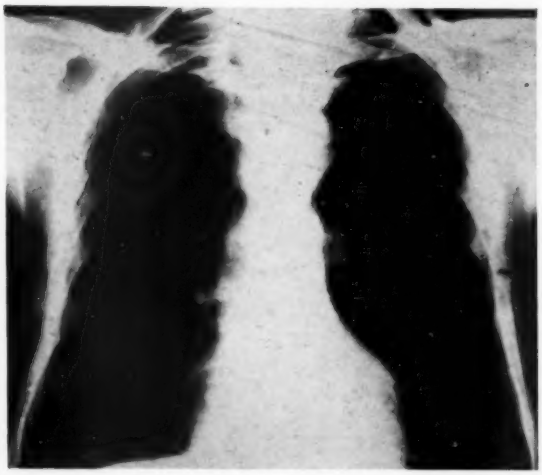

FIG. 15. Upper mediastinal abscess caused by esophageal perforation during esophagoscopy. The abscess is represented by a fusiform shadow in the superior mediastinum. The trachea is displaced to the right. Spontaneous drainage through the large esophageal perforation.

perforations of the esophagus was of a gangrenous nature, whether the inflammation was phlegmonous or localized in the form of an abscess. The tissues were markedly discolored and the exudate was greenish-gray and foul. This is due to the

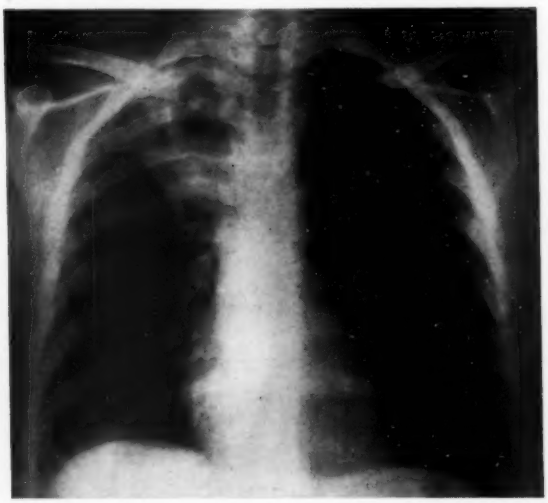

FIG. 16. Foul abscess of superior mediastinum caused by perforation of esophagus by meat bone. Secondary perforation into the lung. The picture is differentiated from that of a simple lung abscess by the fact that the fluid level extends beyond the midline.

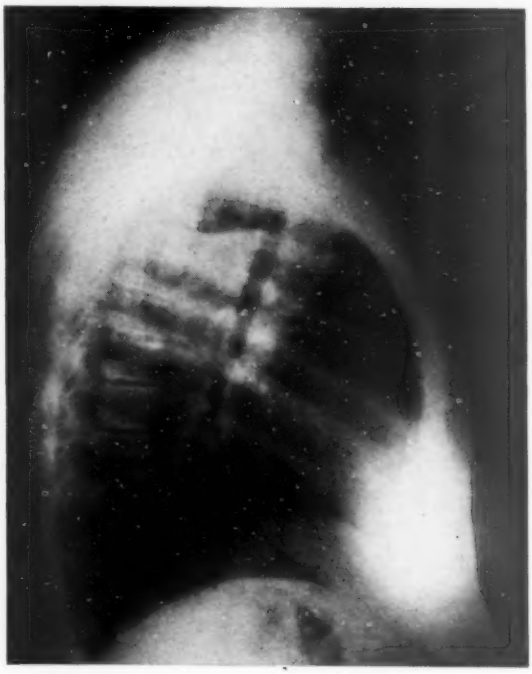

FIG. 17. Same case as in Figure 16. Lateral view showing anterior bowing and displacement of trachea anteriorly.

fact that the infection is caused by a mixture of anaerobic organisms, no doubt similar to those which have their natural habitat in the mouth and throat. The virulence of many of these organisms and their spread into locations removed from the surface

FIG. 18. Gangrenous abscess in paravertebral portion of right lower lobe perforating into the mediastinum. The infection laid bare the bodies of the vertebrae, the aorta, and the esophagus.

causes these infections to assume a fulminating character.

Because of the putrefactive property of the organisms, there soon occurs destruction of considerable areas of tissue and their rapid liquefaction. Abscess formation, therefore, takes place very soon after the esophageal perforation. Because of the extreme virulence of the infection, however, the abscess usually does not remain localized for any considerable period of time, but spreads throughout the mediastinal tissues in the form of a gangrenous phlegmon. Similarly, perforation into the lung or into the pleura may take place early in the course of the mediastinitis.

The perforation through the wall of the esophagus may permit the entrance of air into the mediastinal tissues. The spread of this air along the fascial planes to the root of the neck soon gives rise to a subcutaneous emphysema. This is of considerable significance pathologically, because the air passing through the tissues carries particulate material containing great numbers of organisms which thus cause an extensive gangrenous phlegmon in a short period of time. Extension of the infection occurs therefore not only by contiguity and by way of the lymphatics, but also along the fascial planes wherever the air makes its way.

Fig. 19. Huge mediastinal abscess following the acute pharyngitis complicated by cervical abscess. Perforation into lung and pleura. The picture is differentiated from pyopneumothorax by the fact that the fluid level extends beyond the trachea.

Fig. 20. Same case as in Figure 19. Lipiodol injected into the wound enters the mediastinum. Recovery following drainage of the mediastinum and adjacent pleura.

ROENTGEN FEATURES

A knowledge of the pathogenesis and pathological picture of mediastinitis not only explains its varied roentgen features but also aids in the diagnosis of its different forms. Although it is true that it is not always possible to differentiate these by the roentgen examination alone, an interpretation based upon the knowledge of the pathology will usually be found to be accurate. The exceptions may be recognized from the clinical course of events if the classification, causes and pathological picture of mediastinitis are clearly understood.

1. *Mediastinal Lymphadenitis.* Usually the roentgen examination of the chest does not disclose the presence of moderately enlarged lymph nodes, so that in most of the cases of acute mediastinal lymphadenitis no abnormalities are discernible on the film. Where the nodes are greatly enlarged, how-

FIG. 21. Loculated pyopneumothorax. Although the fluid level extends beyond the midline this is differentiated from a mediastinal abscess by the fact that the mediastinal structures and trachea are displaced to the other side so that the fluid level does not cross them.

ever, they may cause a widening of the mediastinal shadow. Because of the shape of the enlarged lymph nodes which cause this widening, the shadow presents lobulated borders. Occasionally the enlarged paratracheal nodes may be observed as discrete shadows whose origin is unmistakable, and at times the shadows of the enlarged tracheobronchial lymph nodes are seen clearly outlined near the roots of the lungs.

A marked widening of the superior mediastinal shadow with bulging borders, simulating an expanding abscess, may be caused by extremely large suppurating mediastinal lymph nodes which have become matted together by exudate to form a mass. Although this may be undifferentiable from the picture of an abscess of the superior mediastinum, in most cases the convex outlines of the individual nodes produce a scalloped or lobulated border which is never observed in abscess of the mediastinum. It is rarely possible to observe inflamed lymph nodes in the lower portion of the mediastinum, although it is conceivable that films made in the oblique positions may occasionally disclose them. In questionable cases, it may be assumed that the spontaneous resolution of the process indicates that it was in the nature of a mediastinal lymphadenitis.

2. *Phlegmonous Mediastinitis.* In the early stages of phlegmonous mediastinitis and in certain fulminating cases in which there is a rapidly spreading lymphangitis with comparatively little exudate in the mediastinal connective tissue itself, the roentgenogram may disclose no abnormality. In the latter instance there may be seen only the evidences of spread to the lymphatics of the lung and pleura, such as strand-like shadows spreading from the hilum into the lungs, representing a suppurating lymphangitis, or roentgen evidence of a bilateral pleuritis. In most of the cases, however, there soon appears a diffuse widening of the superior mediastinal shadow. The structures that make up the normal borders of the mediastinum become poorly differentiated, the contour of the widened mediastinum becomes straight and usually presents sharply demarcated vertical borders. The uppermost portions of the medi-

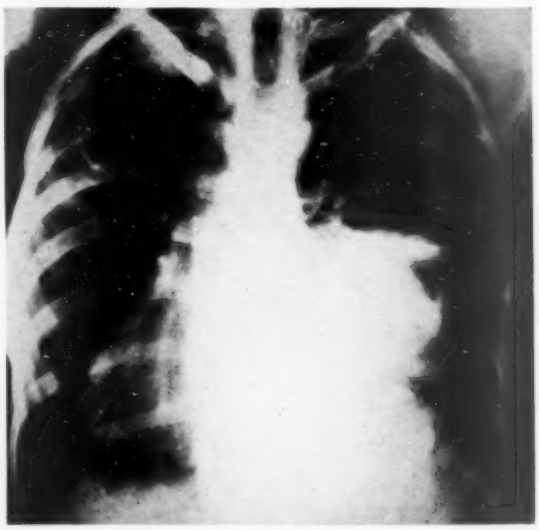

FIG. 22. Lower mediastinal abscess following upper respiratory infection. The roentgen shadow is undifferentiable from that of an empyema of the paramediastinal pleura. However, the enlargement of the right paratracheal lymph nodes suggests the presence of mediastinitis.

astinal borders are of particular interest. These appear to spread outward over the apex of the lung. This unusual appearance is undoubtedly due to a depression of the mesial borders of the pleural cupolas over the apex of the lung by inflammatory exudate.

There is a general increase in density of the superior mediastinal shadows. If the length of exposure of the film to the roentgen rays is not increased, the trachea is not as clearly defined as in the normal chest and the aortic knob is poorly visualized or may not be outlined at all. Care must be taken that the film be exposed during the phase of complete inspiration if error is to be avoided, for as is well known, the mediastinal shadow becomes considerably widened during expiration. It is advisable in cases suspected of mediastinitis to make films of the neck in the lateral position. In cases where the mediastinal widening is minimal, the finding of a widened retrotracheal (prevertebral) shadow may establish by inference the diagnosis of mediastinitis.

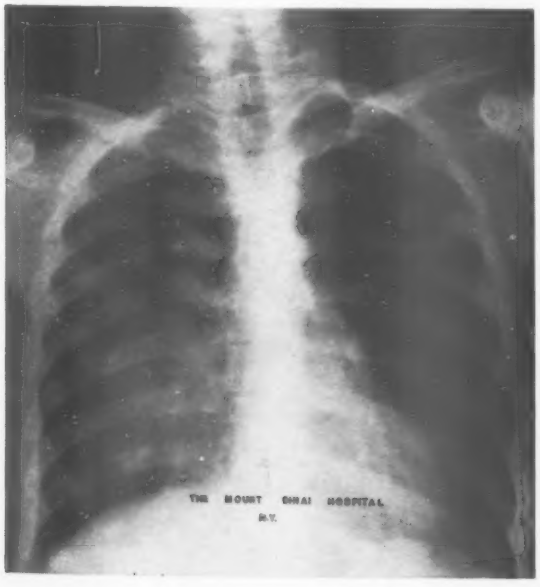

Fig. 23. Lower mediastinal abscess simulating empyema. This complicated mastoiditis, pneumococcus Type I. Recovery following posterior mediastinotomy during which the vertebrae and the aorta were exposed.

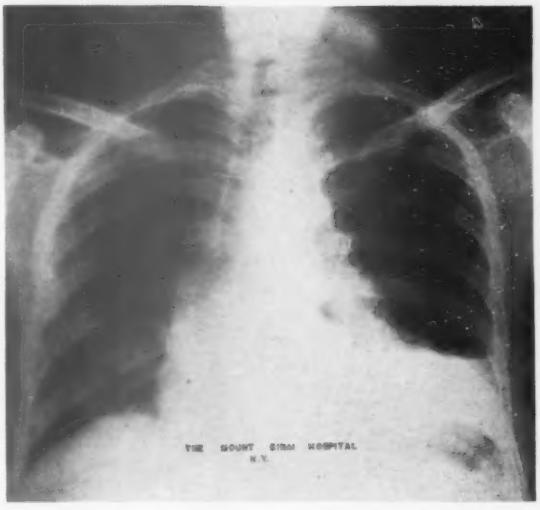

Fig. 24. Pyopneumothorax following perforation of lower esophagus through the overlying pleura. This was accompanied by a local area of gangrenous mediastinitis.

In the lower mediastinum, a diffuse inflammation is even less readily recognizable on the roentgenogram. Although it is logical to assume that the inflammatory process should cause a partial obscuration of the lower posterior mediastinal space on the oblique lateral views, the absence of a shadow with a sharp outline and the great variation in the degree of illumination of this region are factors which make any accurate interpretation concerning the presence of inflammation of this portion of the mediastinum impossible from the roentgen examination.

3. *Mediastinal Abscess.*

a. Abscess of the Superior Mediastinum. In the earliest stages of abscess of the upper mediastinum, the roentgen picture may simulate that of phlegmonous mediastinitis, but the rapid widening of the shadow and the formation of a bulging border usually will soon establish the diagnosis. When there is any doubt concerning the roentgen differentiation between phlegmonous mediastinitis and abscess of this portion of the mediastinum, a history of the presence of an abscess in the neck will make the diagnosis clear, for as has been stated, an abscess of the neck is usually followed by a medias-

Fig. 25. Upper mediastinal abscess following acute pharyngitis complicated by a cervical abscess. The mediastinal abscess is represented by only a moderate widening of the mediastinum.

tinal abscess. It may therefore be stated categorically that the presence of a shadow in the superior mediastinum following upon or concomitant with an abscess of the neck indicates the presence of an abscess in the mediastinum.

Although there may be convex borders on both sides, the bulge of the abscess is usually noted on the right. This is due partly to the fact that the aorta obscures the shadow of the mediastinal abscess on the left side, and partly to the fact that the abscess in its development has a tendency to spread on the right side of the mediastinum. Since mediastinal abscesses are practically always situated in the posterior mediastinum, there will be noted an anterior displacement of the trachea within the chest, as well as within the neck. This will be disclosed on films made in the lateral position. At times this displacement is so extreme as to produce an anterior bowing of the trachea as seen in this position. Since the abscess is situated essentially behind the trachea there is rarely a displacement of this organ to either side.

b. Abscess of the Inferior Mediastinum. An abscess of the lower mediastinum that extends to the right side causes a semicircular shadow projecting into the right pulmonary field. This cannot be differentiated roentgenologically from an empyema of the mesial portion of the pleural cavity. An abscess which extends to the left may easily be overlooked on casual roentgen examination because of its relation to the heart. Careful inspection of the cardiac shadow will often disclose its presence, especially if the film is somewhat overexposed. The mediastinal abscess can be plainly visualized, however, if it is large enough to extend beyond the heart or if the examination is made in the left oblique position.

c. Mediastinal Abscess Complicating Perforation of the Esophagus. The presence of a widened mediastinal shadow following the occurrence of an accident that is capable of producing an esophageal perforation is presumptive evidence that a mediastinal abscess is present. Similarly, the occurrence

Fig. 26. Same case as in Figure 25. Lateral view showing the widening of retrotracheal and retropharyngeal space of the neck. The widening is not appreciable behind the thoracic trachea.

of roentgen evidences of mediastinal or subcutaneous emphysema following injury to the esophagus is indicative indirectly of the presence of a mediastinal abscess. Within a short time this may be complicated by the presence of a phlegmon for, as already stated, it may justifiably be assumed that a localized area of suppuration is already present within a short time after the perforation.

Occasionally the globular shadow of an abscess in the mediastinum exhibits a fluid level, indicating the presence of a localized collection of pus and air.

Radiopaque foreign bodies which have caused the perforation may be visualized on the ordinary roentgenogram, but are better seen in examinations of lateral views of the neck and of oblique and lateral views of the mediastinum. Non-opaque foreign bodies may sometimes be recognized by the adherence to them of ingested barium. Occasionally ingested radiopaque contrast media may be demonstrated to enter the mediastinal abscess through the perforation in the esophagus.

d. Mediastinal Abscess Perforating into the Lung. The early picture of a mediastinal abscess perforating into the lung is that of a localized area of pneumonic consolidation adjacent to the mediastinum. Soon the consolidated lung liquefies, but as yet the roentgen picture remains unchanged unless there is a free communication with the esophagus, in which case the entrance of air into the secondary lung abscess causes the formation of a fluid level. In any event, a cavity with a fluid level will form as soon as the abscess ruptures into a bronchus.

Fig. 27. Phlegmonous mediastinitis following acute pharyngitis. Rapid course terminating in death. The increase in the pulmonary markings is due to a pneumonia characterized by suppurative lymphangitis of the lungs.

Fig. 28. Same case as in Figure 27. Lateral view showing widening of the retrotracheal space.

The abscess cavity represents a combination of mediastinal abscess together with the adjacent lung abscess—the fluid level, therefore, is situated not only within the lung but also within the mediastinum. Since the right side of the trachea extends approximately to the border of the mediastinum, the fluid level will be seen to pass beyond this border. The crossing of the trachea by a horizontal fluid level will serve to differentiate a mesially situated lung abscess or a localized pyopneumothorax from a mediastinal abscess which has perforated into the lung.

e. Perforation of Mediastinal Abscess into the Pleura. Occasionally an unrecog-

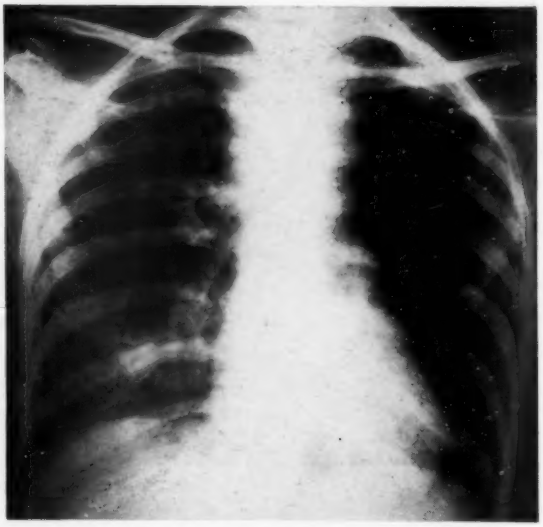

Fig. 29. Phlegmonous mediastinitis following acute pharyngitis. Rapid course terminating in death. Suppurative pneumonia of the lower lobe.

nized mediastinal abscess perforates the pleura to cause an empyema. In the case of large esophageal perforations, a pyopneumothorax may result. Unless this is associated with evidence of emphysema of the mediastinum or at the root of the neck, the origin in the mediastinum cannot be suspected from the ordinary roentgen picture. Although we have not had the occasion to make the observation in any of the cases of our series, it is conceivable that the ingested iodized oil may enter the pleural cavity in such an instance and thus demonstrate the pathogenesis of the pyopneumothorax.

More frequently the empyema results from the perforation of an abscess which does not communicate with the esophagus. If such an empyema is confined by adhesions it is limited to the mesial portion of the pleural cavity. It cannot be differentiated roentgenologically from an empyema secondary to disease of the lung except when outlined by the injection of iodized oil.

CLINICAL MANIFESTATIONS

A discussion of the variety of clinical manifestations which were encountered in our series of cases would be beyond the scope of our paper. However, two statements can and should be made in this place. First and most important, the textbook picture of suppurative mediastinitis is only rarely seen. We refer to the description in textbooks of recurrent chills, high fever, profound prostration, severe toxemia, typhoid state, etc. When present, these manifestations are observed only in the advanced stages of the mediastinal infection. Secondly, textbooks refer to interference with circulation as a sign of mediastinitis. In only one instance in our series, an abscess of the anterior mediastinum under great tension, was there evidence of such interference.

Clinically, our cases of suppuration in the mediastinum can be classified into fulminating, moderately severe, and relatively mild types. The fulminating cases, usually fatal within a few days, presented either the rare textbook picture of overwhelming sepsis just referred to, or, much more commonly, dysphagia, dyspnea, and later, the picture of a severe "pneumonia." In all our fulminating cases either a throat infection

Fig. 30. Same case as in Figure 29. Lateral view of neck showing minimal degree of retrotracheal widening.

with or without a retropharyngeal abscess, or an esophageal trauma, was the etiological factor. In most of the cases a diffuse phlegmonous mediastinitis was found at autopsy, but the clinically significant point is that localized suppuration was noted in a few instances, and such cases may therefore have been amenable to operative relief.

Cases of moderate severity may also be of non-traumatic as well as of traumatic origin. In our series all cases were fatal when the source was non-suppurative or, if suppurative, when the causative abscess had not been adequately evacuated. The duration was from a week to a month or longer. Beginning with sore throat, fever, and chill in the non-traumatic group, and with pain in the neck and chest, dysphagia and fever in the traumatic variety, the course in both was characterized by moderate toxemia and dysphagia. Of greatest significance in the symptomatology was the occurrence of a deceptive remission in the fatal cases. Its deceptive aspect cannot be too strongly stressed. The period of apparent improvement sometimes was definite and clean cut, with subsidence of fever and dysphagia, disappearance of spinal tenderness, and return of a feeling of well being. Indeed, there were 3 cases in which operation unfortunately was deferred because a remission, interpreted as spontaneous subsidence, had set in.

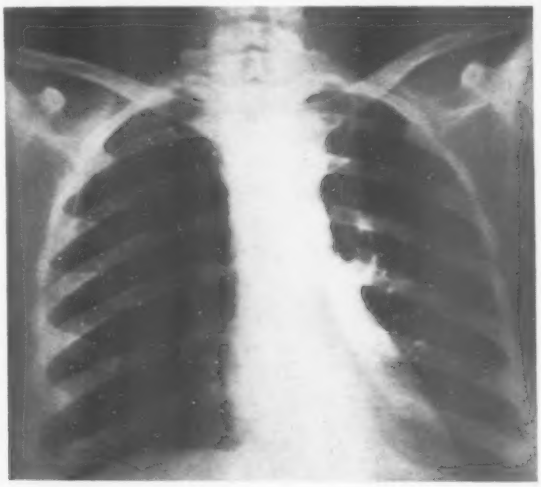

Fig. 31. Diffuse mediastinal lymphadenitis; spontaneous cure. First film made after two weeks of fever, choking sensations and dysphagia, shows a diffuse widening of the mediastinum. There was no cervical abscess.

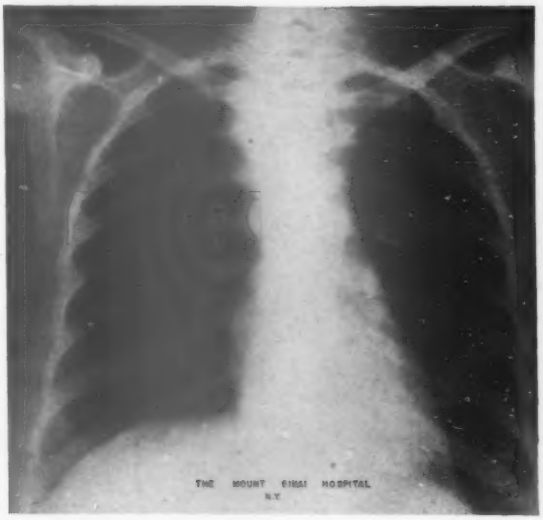

Fig. 32. Same case as in Figure 31. Four and a half weeks after onset. The bulging right border of the mediastinum suggests abscess formation. In view of its later recession, it is assumed that this is caused by markedly inflamed lymph nodes.

An important group of cases, by no means

Fig. 33. Same case as in Figures 31 and 32. Six and a half weeks after onset. Recession of mediastinal borders indicating resolution of the process. The patient eventually recovered completely.

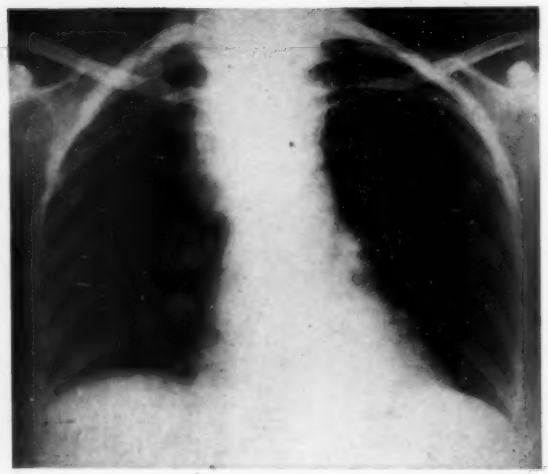

FIG. 34. Mediastinal lymphadenitis; spontaneous cure. First film made after one month of septic fever as high as 106° F., associated with chills, in the course of an upper respiratory infection. The bulging of the mediastinum suggests the presence of an abscess, but the lobulation of the border indicates enlargement of the lymph nodes. There was no cervical abscess.

rare, and remediable by operative treatment, is that in which the expectoration of pus, usually foul, occurred, to be followed by a remission in other symptoms. In such cases the mediastinal abscess had burrowed its way through the lung and broken into a bronchus. There should be no difficulty in the recognition of these cases and the roentgenogram is apt to be characteristic. The etiology was perforation of the esophagus in 6 of 8 cases in our series. In all 6 the pus which was expectorated was as foul smelling as in putrid pulmonary abscess.

The third group, with relatively mild clinical course, presented a suppurative mediastinal lesion in all instances, and this was invariably a well localized abscess. In all cases an abscess in the cervical region had been present, and fever had continued without a discernible local cause after the cervical abscess had been drained. Dyspnea, cough, or pain called attention to an intrathoracic complication. Nevertheless, the substantial globular shadow which was disclosed on the roentgenogram in these cases was for the most part unexpected.

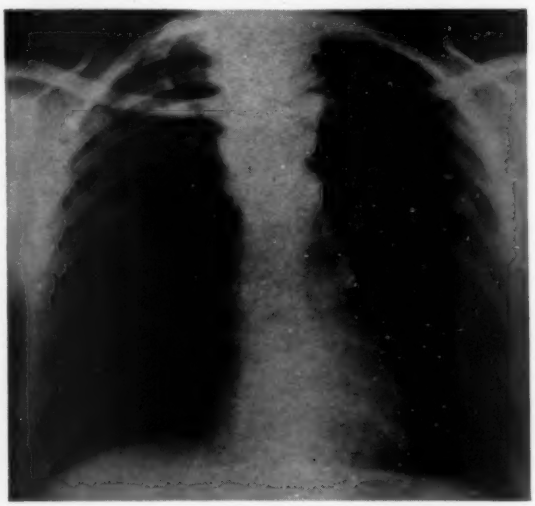

FIG. 35. Same case as in Figure 34, two weeks later. Marked recession of the mediastinal borders; the tendency to lobulation persists. The patient eventually recovered spontaneously.

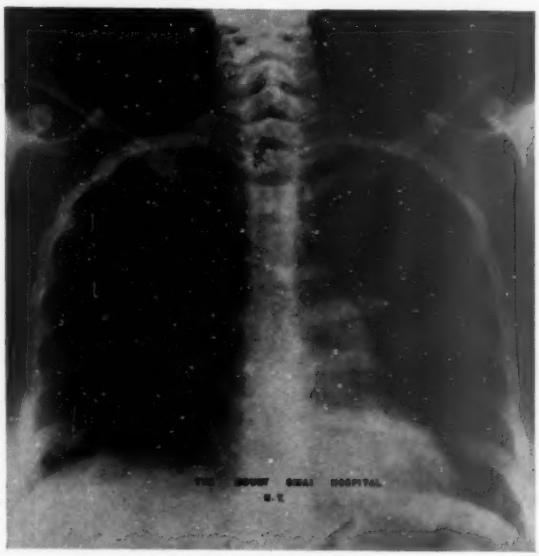

FIG. 36. Mediastinal lymphadenitis complicating upper respiratory infection. Enlarged paratracheal and tracheobronchial lymph nodes after one month of fever. The nodes eventually disappeared as the patient recovered. No cervical abscess.

There exist several varieties of cases in which clinical manifestations referable to the mediastinal infection do not exist. They cannot be discussed because of the limitation of time.

The symptomatology outlined in the

three main groups comprises more particularly a clinical picture of suppuration in the posterior mediastinum. A pleural infection may supervene in any case of suppuration in the posterior mediastinum, but it occurs more regularly and characteristically in diffuse phlegmonous posterior mediastinitis. By way of contrast, the much rarer instances of suppuration in the anterior mediastinum are not complicated by pleural infection.

A difficult subject for discussion, and one on which we can offer but little constructive comment, is that of the symptomatology of non-suppurative acute infections of the mediastinum. As an example of the difficulty in recognition we may cite two instances of spontaneous recovery (presumably without pus formation) in which the clinical manifestations and the roentgen features were identical with those we have noted in mediastinal abscess of moderately severe grade. In both there were anterior displacement of the trachea and clearly indicated mediastinal shadows on the film. The ready recognition of the non-suppurative variety of mediastinal infection generally termed "mediastinal lymphadenitis" is of course a different matter, especially when a characteristic roentgenogram is seen.

DIAGNOSIS

The physical examination of the chest is essentially negative in most instances of acute mediastinal infection except for the signs of pleural effusion or of pneumonic infiltration when such complications exist. Spinal percussion tenderness is a suggestive diagnostic sign, but this disappeared despite the persistence of spread of a posterior mediastinitis in two instances in our series. We have seen the normal passage of a barium meal in proved mediastinitis. The waxing and waning of physical signs render them singularly unreliable as diagnostic features. On the other hand, examination of the neck may yield definitive information when a mediastinal infection is derived from the cervical region. Infiltration and tenderness are often but not invariably present in traumata to the cervical esophagus; in some instances crepitation is to be noted. A shift of the trachea is of greatest diagnostic significance. It is always displaced forward when a mediastinal infection is derived from an infection deeply situated in the lower cervical region. From the foregoing it is obvious that the diagnostic features which have been mentioned are not to be compared with the information to be derived from the roentgenogram. Undoubtedly, the correct diagnosis of a potential or of an existent mediastinal infection would be made more often if the erroneous impression of its rarity were discarded and the likelihood of its development following injuries to the esophagus or infections in the deep cervical planes were borne in mind.

INDICATIONS FOR OPERATION

Probably the most important operative indication is prophylactic and is concerned with the lesion which frequently precedes the mediastinal infection. Traumatic penetration of the esophagus was the etiology in almost one-half of our cases. As a result of our experiences we are convinced that an operation consisting in exposure of and drainage to the laceration in the esophagus is imperatively indicated in most cases despite the possibility of spontaneous recovery, and regardless of the situation of the tear. A consideration of the unlikelihood of healing about a perforated esophagus, the insidious manner in which the mediastinum becomes infected, the difficulties in diagnosis, and the high mortality when mediastinitis is fully developed, should lead to the decision to operate in most cases even though the patient may be largely symptom-free at the time.

Cervical infection of non-traumatic origin was the source of the mediastinal infection in about one-third of our cases. Adequate and timely drainage would have obviated at least some of the cases of mediastinal infection. Special reference should be made to a small but important group of cases of retropharyngeal abscess in children which were not recognized by the custom-

ary methods of examination (digital, pharyngoscopic, esophagoscopic) although suspected because of the history. Lateral roentgenograms of the neck established the correct diagnosis in a number of instances. There were several tragic cases in which exploration through an external incision was warranted on clinical grounds with supporting roentgenographic evidence of the existence of a retropharyngeal lesion, but which was not disclosed until autopsy. The latter revealed a cervical abscess with extension into the mediastinum in these cases.

PRINCIPLES OF OPERATIVE TREATMENT

Although a discussion of operative technique would be out of place, certain principles in the operative treatment should be enunciated, particularly those which involve roentgenologic cooperation. With roentgenographic evidence of a widened retrotracheal space, a cervical approach is warranted in cases of posterior mediastinitis derived from the neck even though an additional thoracic approach might be required. In this cervical approach the sternomastoid muscle and carotid sheath are drawn laterally, the thyroid lobe mesially, and the dissection deepened to the lateral wall of the esophagus. If pus is not encountered at this stage the guides to the further dissection for the suppurative focus should be the presence of inflammatory exudate in the operative field and the preoperative lateral roentgenogram of the neck. The site of the collection of pus encountered in the neck should be the lead to be followed for the entry of the mediastinum (posterior superior mediastinum). Drainage of the latter via the neck may be adequate down to the bodies of the second, third, or possibly the fourth dorsal vertebrae, but according to our experience, will not be adequate below these levels. A posterior mediastinotomy should be added, therefore, in cases in which further descent is suspected.

The operative approach to the posterior mediastinum should be based on painstaking efforts at localization of the lesion by physical signs, esophagoscopy in some of the perforative lesions, but above all by precise roentgenological studies. Patients are usually too ill to withstand any more or less formal posterior mediastinotomy. Exploratory puncture is probably a questionable procedure when the evidence points to a deeply placed collection of pus in the mediastinum. Unnecessary entry of what may be a completely uninvolved pleural cavity should certainly be avoided. In short, the roentgenogram is the basic guide for correct approach to the mediastinal abscess, and no positions from which roentgenographic information as to the exact site of the lesion may be obtained should be omitted. Although entry into the mediastinal abscess without entering the pleura was attempted in all our cases, the pleura was traversed in several. It is interesting to note that of the 4 cases in which the pleural cavity was opened and packed off in a one stage drainage of a mediastinal abscess, all recovered without the development of empyema. This is not meant to indicate a belief that the pleura can be traversed with impunity for the drainage of a mediastinal abscess. It refutes, however, a statement which has been made concerning inevitable death from fulminating empyema under such circumstances.

Again because of roentgenographic features, special reference should be made to the surgical problem of a mediastinal abscess which has ruptured into the lung. The film is the guide to the existence of the pulmonary invasion; a fluid level is seen to extend laterally, in some instances, to a considerable distance from the median line. Under the latter circumstances the operative approach may be made directly over the abscess of the lung rather than by way of the abscess in the mediastinum.

SUMMARY

The diagnosis of acute mediastinitis and of mediastinal abscess is based largely on roentgenological examination. The latter is the sole means of accurately localizing such lesions for surgical purposes. Acute mediastinitis will often remain undiagnosed or

untreated if roentgenograms are not made or if its roentgenological features are not understood. Some knowledge of the pathology and the clinical manifestations is necessary for the correct interpretation of films.

Three classifications of acute mediastinitis are made: pathological, etiological, clinical. The pathogenesis is set forth with particular reference to acute infections of the pharynx and injuries to the cervical esophagus. The pathology of mediastinal lymphadenitis, phlegmonous mediastinitis, and mediastinal abscess is described. The special features of mediastinal infection secondary to perforation of the esophagus, and of perforation of mediastinal abscess into the lung, are outlined.

The roentgen features of mediastinal lymphadenitis, phlegmonous mediastinitis, and of abscesses in the superior and inferior mediastinum are detailed. Special reference is made to mediastinal abscess derived from esophageal perforation and to mediastinal abscess perforating into the lung or pleura.

A general survey of the clinical manifestations of mediastinal infection is presented, based on the cases which were studied and not on the literature. The textbook characteristics of acute mediastinitis were rarely seen. The contrast between large mediastinal abscesses and mild clinical features was emphasized.

The indications for operation and the general principles of operative treatment are discussed.

THE ROENTGENOLOGIC DIFFERENTIATION OF RHEUMATIC FROM NON-RHEUMATIC MITRAL VALVE CALCIFICATIONS*

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BROOKLYN, NEW YORK

CALCIFICATIONS of the mitral valve may occur either in its leaflets, its annulus fibrosus or occasionally in both structures. These are demonstrable roentgenoscopically if sufficient calcific material is present, and in many cases roentgenograms can be made with equipment of sufficient capacity. Roentgenoscopic visualization is much easier than their roentgenographic demonstration, inasmuch as the dancing motion imparted to the calcifications by the heart action is a cardinal diagnostic point.

Mitral leaflet calcifications usually occur on the basis of pre-existent rheumatic heart disease. Patients so afflicted give a history indicative of a previous rheumatic infection and very often of diminished cardiac reserve. On physical examination a systolic and diastolic murmur may be heard over the apex of the heart in patients with lesions limited to the mitral valve. Multiple valve lesions involving the aortic and tricuspid as well as the mitral valve are frequent, and produce their characteristic murmurs. The murmurs may be altered if auricular fibrillation is present. Mitral valve calcifications indicate an advanced lesion in most cases.

Calcific deposits in the annulus fibrosus are relatively benign. They occur chiefly in elderly individuals who present neither clinical evidences nor physical findings of organic valvular heart disease. In most cases the finding is incidental and of no immediate prognostic importance.

Calcifications in the annulus fibrosus have been described as large deposits of an O, U or J shape in the posterior third of the heart shadow. Deposits in the bodies and free edges of the valve leaflets supposedly are smaller and of a more diffuse nature. Beyond this, the roentgenologist encounters difficulty in making a differential diagnosis. Inasmuch as the extent of the calcifications may vary considerably from patient to patient, a method which would assist in making a differential diagnosis roentgenologically would be helpful. Although this may readily be accomplished by restudy of the clinical findings after the calcifications have been identified roentgenologically, it should be within the province of the roentgenologist to make the diagnosis on the basis of his findings alone.

In order to investigate this possibility, the roentgenoscopic, clinical and postmortem findings of 25 patients with calcified mitral valves on a rheumatic basis were compared with those of 9 patients with calcifications limited to the annulus fibrosus of the mitral valve.

RHEUMATIC MITRAL CALCIFICATIONS (TABLE I)

The youngest patient in this group was thirteen years old, the oldest was sixty-two. The extent of the calcifications was such that the lesions might have been identified on roentgenoscopic study had they been sought. This was done in the last 5 cases, and the lesion was readily identified. In each instance the deposits were limited to the bodies and free edges of the leaflets.

Valve Lesions. Advanced deformity of the mitral orifice was found in each patient. Twenty-three had mitral stenosis and insufficiency, and 2 had mitral stenosis. Concomitant defects of the aortic or tricuspid valves were common.

Roentgenoscopic Findings. The accuracy

* From the Radiologic Service of A. J. Bendick, M.D., Montefiore Hospital, New York, and the Radiologic Service of M. G. Wasch, M.D., the Jewish Hospital of Brooklyn, Brooklyn, N. Y.

TABLE I

RHEUMATIC MITRAL VALVE CALCIFICATIONS

Case Number	Age	Sex	Left Auricle	Left Ventricle Thickness mm.	Right Auricle	Right Ventricle Thickness mm.	Heart Weight gm.	Valve Lesions	Congestive Heart Failure	Degree of Mitral Valve Calcification
1	13	M	Marked	Slight 13 mm.	Marked	Marked 6–9 mm.	450	M.A., M.I., A.I.	Advanced	Marked
2	15	M	Marked	Slight 15 mm.	Marked	Marked 7 mm.	350	M.S., M.I., T.S., T.I., A.I.	Advanced	Moderate
3	27	F	Marked	Marked 27 mm.	Marked	Marked 8 mm.	730	M.S., M.I., A.I.	Advanced	Marked
4	22	F	Marked	None 10 mm.	Marked	Marked 7 mm.	425	M.S.	Advanced	Moderate
5	21	M	Marked	Marked 18 mm.	Moderate	Marked 8 mm.	500	M.S.	Advanced	Marked
6	24	F	Marked	Marked 18 mm.	Moderate	Marked 9 mm.	550	M.S., M.I., T.I.	Advanced	Marked
7	35	F	Marked	Moderate 17 mm.	Moderate	Moderate 4 mm.	760	M.S., M.I., T.I.	Advanced	Marked
8	30	F	Marked	Marked 19 mm.	Moderate	Marked 7 mm.	500	M.S., M.I., T.I., T.S.	Advanced	Marked
9	35	F	Marked	Slight 11 mm.	Moderate	Moderate 4 mm.	440	M.S., M.I., T.I.	Advanced	Advanced
10	37	F	Marked	Moderate 14 mm.	Marked	Marked 5 mm.	600	M.S., M.I.	Advanced	Advanced
11	38	M	Marked	Slight 13 mm.	Marked	Marked 5 mm.	460	M.S., M.I.	Advanced	Advanced
12	47	M	Marked	Marked 19 mm.	Marked	Marked 5 mm.	720	M.S., M.I., A.I.	Advanced	Advanced
13	40	F	Marked	Marked 22 mm.	Marked	Marked 8 mm.	700	M.S., M.I.	Advanced	Moderate
14	45	M	Marked	Moderate 14 mm.	Marked	Marked 10 mm.	580	M.S., M.I.	Moderate	Marked
15	48	F	Marked	Slight 14 mm.	Moderate	Marked 8 mm.	300	M.S., M.I.	Advanced	Marked
16	40	F	Marked	Moderate 15 mm.	Moderate	Moderate 4 mm.	550	M.S., M.I.	Advanced	Marked
17	47	F	Marked	Marked 19 mm.	Marked	Marked 5 mm.	720	M.S., M.I., A.I.	Advanced	Marked
18	46	F	Marked	Slight 12 mm.	Moderate	Marked 8 mm.	420	M.S., M.I., T.I.	Advanced	Marked
19	43	F	Marked	Marked 18 mm.	Moderate	Marked 6 mm.	650	M.S., M.I.	Advanced	Marked
20	50	F	Marked	Slight 12 mm.	Moderate	Moderate 4 mm.	500	M.S., M.I.	Advanced	Moderate
21	55	M	Marked	Marked 22 mm.	Slight	Moderate 5 mm.	550	M.S., M.I.	Advanced	Moderate
22	56	F	Marked	Marked 22 mm.	Moderate	Marked 6 mm.	750	M.S., M.I., A.I.	Advanced	Marked
23	62	M	Marked	Slight 12 mm.	n.m.*	Marked 5 mm.	850	M.S., M.I., A.I.	Advanced	Marked
24	55	M	Marked	Marked 21 mm.	Slight	Moderate 5 mm.	550	M.S., M.I.	Advanced	Marked
25	49	F	Marked	Moderate 17 mm.	n.m.	Marked 8 mm.	620	M.S., M.I., A.S., A.I.	Advanced	Marked

* n.m.—not mentioned on protocol.

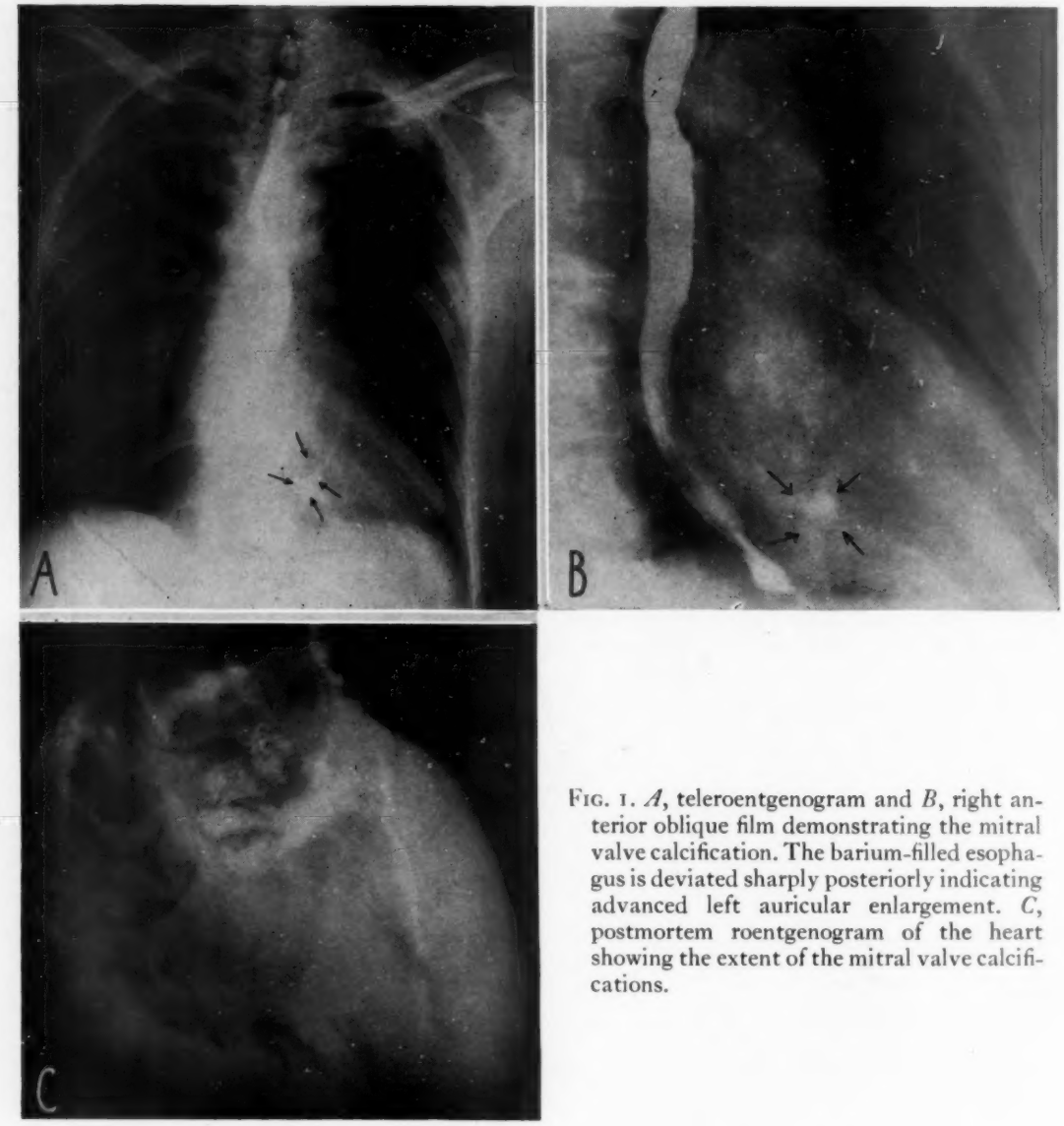

Fig. 1. *A*, teleroentgenogram and *B*, right anterior oblique film demonstrating the mitral valve calcification. The barium-filled esophagus is deviated sharply posteriorly indicating advanced left auricular enlargement. *C*, postmortem roentgenogram of the heart showing the extent of the mitral valve calcifications.

of the roentgenoscopic estimation of the size of the various chambers of the heart was borne out by comparison with the autopsy findings. The outstanding fact was that each patient had marked *left auricular enlargement*. This was readily diagnosed by inspection of the barium-filled esophagus with the patient in the right anterior oblique position. The degree of posterior deviation of the esophagus roughly parallels the size of the left auricle. Elevation of the left main bronchus as seen with the patient in the left anterior oblique position, or the presence of the left auricular shadow on the right cardiac border are also excellent indices of left auricular enlargement.

The anterior surface of the *right ventricle* was quite prominent in each instance, a finding readily obtained by roentgenoscopic examination of the patient in the right anterior oblique position. The main trunk of the pulmonary artery and the conus also were definitely exaggerated.

The *left ventricle* showed varying degrees of enlargement. Those patients with mitral lesions predominantly of a stenotic nature

showed no or little enlargement of the left ventricle, while patients with aortic lesions with or without mitral insufficiency showed definite left ventricular enlargement.

The *right auricle* was appreciably enlarged in most patients.

The weight of the heart did not appear to be related either to the valve lesion or the presence of calcifications.

Every patient in this series had advanced congestive heart failure.

NON-RHEUMATIC MITRAL VALVE CALCIFICATIONS (TABLE II)

The youngest patient in this group was fifty-seven years old. In each instance the degree of calcification was such that the lesion could have been seen roentgenoscopically, and was visualized in the last 2 patients. The deposits were located in the annulus fibrosus of the valve.

Valve Lesions. One patient had mitral insufficiency, probably secondary to an old hypertension since no rheumatic stigmata were found. The others had anatomically and functionally competent valves. No murmurs which might be considered diagnostic were noted during life.

Fig. 2. Teleroentgenogram showing calcification of the annulus of the mitral valve. Roentgenoscopic study with the patient in the right anterior oblique position showed the esophagus to pursue its normal course. No left auricular enlargement is present.

Roentgenoscopic Findings. Three patients had slight enlargement of the left auricle. All three had definitely enlarged left ventricles secondary to hypertensive heart disease. It is quite possible that the left auricular enlargement seen roentgenoscopically was due to a shift in the position of the left auricle caused by the left ventricular en-

Table II

NON-RHEUMATIC MITRAL VALVE CALCIFICATIONS

Case Number	Age	Sex	Left Auricle	Left Ventricle Thickness—mm.	Right Auricle	Right Ventricle Thickness—mm.	Heart Weight gm.	Valve Lesion	Heart Failure	Blood Pressure
1	79	F	Slight	Marked 20 mm.	None	None 3 mm.	320	M.I.	None	190/88
2	68	F	None	Slight 10 mm.	None	None 2 mm.	300	None	None	Normal
3	73	M	None	Slight 15 mm.	None	None 4 mm.	350	None	None	170/90
4	75	F	None	Marked 20 mm.	None	None 3 mm.	350	None	None	Normal
5	75	F	None	Slight 15 mm.	None	None	420	None	None	160/110
6	65	M	None	Moderate n.m.*	None	None n.m.	480	None	Congestive heart failure —2 yr.	200/110
7	57	M	None	Marked 25 mm.	None	None 4 mm.	510	None	None	210/110
8	57	M	Slight	Moderate 17 mm.	None	Marked 6 mm.	550	None	Congestive heart failure —3 yr.	175/115
9	69	F	Slight	Marked 20 mm.	None	None	640	None	None	190/88

* n.m.—measurement not mentioned in autopsy protocol.

largement. The others presented no evidences of left auricular enlargement.

Right ventricular enlargement was present in one patient who had hypertension and congestive heart failure. The others showed no right ventricular enlargement.

SUMMARY

Roentgenoscopic study of every patient in this series with calcified rheumatic mitral valve disease presented definite evidences of enlargement of the left auricle and right ventricle. Those with calcific deposits limited to the annulus fibrosus, however, did not present a constant pattern of chamber enlargement. The basis for these findings is that the patients with rheumatic mitral disease with calcifications had advanced valvular deformities which produced characteristic cardiac chamber enlargements, while those with calcifications in the annulus fibrosus had competent valves.

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Vol. 44, No. 5

PROGNOSIS IN SILICOSIS*

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THE importance of silicosis has been emphasized by its inclusion in many states among compensable occupational diseases. The public health and medical aspects of the condition are often complicated by complex economic problems. Advance knowledge as to the approximate period of disability and the probable result of treatment is therefore valuable.

This study is a discussion of the factors influencing prognosis and is based on observations in 511 anthracite coal miners, many of whom were rock drillers, admitted as patients to the White Haven Sanatorium complaining of respiratory symptoms. The pulmonary changes in these workers, known as anthracosilicosis, were the result of the inhalation of a mixture of coal and rock dust. Most of them had been exposed at frequent intervals to high concentrations of silica particles, so that the lesions found resemble more closely those due to pure silicosis rather than simple anthracosis. This is in accordance with the view expressed by Dreessen and Jones,[1] who found that although anthracite miners inhale a mixture of dust, the ultimate pulmonary changes are those of silicosis.

Of the 511 miners, 191 died, 77 were discharged as improved, and 243 were unimproved on discharge. We have analyzed the histories of 100 of those who died, of whom 66 came to autopsy, and compared the findings with the 77 who were discharged improved. The findings in both groups have been further studied as to the stage of the disease and the presence or absence of clinical tuberculosis. While statistical analysis of the figures is informative, it is not as instructive as a study of some of the clinical and roentgenologic observations found in the case histories. Some of these findings we have reported earlier, sometimes with other collaborators.[4,5,6,7,8]

In the 100 patients who died, the ages varied from twenty to sixty-nine years; the length of occupation from five to forty-nine years; 10 were in Stage I, 32 in Stage II, and 58 in Stage III of the disease. Of this group, 82 had evidence of tuberculosis, and 75 of these had tubercle bacilli in the sputum. In the remaining 7, the evidence of tuberculosis was found on postmortem examination (Tables I, II and III).

TABLE I

AGE

Years	Improved		Died	
	Number	Per Cent	Number	Per Cent
15–19	1	1.2		
20–29	4	5.2	8	8
30–39	20	25.9	17	17
40–49	30	38.9	42	42
50–59	19	24.6	29	29
60–69	3	3.8	4	4
	77		100	

The ages of the 77 patients discharged as improved varied from fifteen to sixty-nine years; the length of occupation from three to forty years; 9 (11.7 per cent) were classified as Stage I, 29 (37.6 per cent) as Stage II, and 39 (50.6 per cent) as Stage III. In this group, the sputum of 45 patients was positive for tubercle bacilli, and in 32 negative (Tables I, II and III).

Age and length of occupation have, of themselves, no influence on the prognosis, except that with increasing length of occupation, the amount of dust and the accompanying changes increase. The greatest number in both the improved group and the group who died were in the fifth and sixth decades. Occasionally, one sees a younger worker who, as the result of exposure to the

* From the White Haven Sanatorium, White Haven, Pa. Read at the Fortieth Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 19–22, 1939.

TABLE II

LENGTH OF OCCUPATION

Years	Improved		Died	
	Number	Per Cent	Number	Per Cent
Less than 6	5	6.4	2	2
6–10	6	7.7	9	9
11–15	11	12.7	13	13
16–20	15	19.4	26	26
21–25	19	24.6	23	23
26–30	11	12.7	16	16
31–35	4	5.2	5	5
36–40	1	1.2	3	3
41–45			1	1
46–50			2	2
Unknown years	5	6.4		
	77		100	

high concentrations of dust encountered in rock drilling, exhibits marked changes.

Prognosis becomes poorer as the stage of silicosis advances. In the first and second stages of the disease, and in the absence of complications, there is usually a favorable response to rest and routine hospital care. The distressing symptoms frequently disappear with a short period of bed rest, and many patients return to gainful occupations. On the other hand, in Stage III, the ultimate outlook is unfavorable, even though the symptoms may subside rapidly at the beginning of treatment. Many of these patients return home, but as semi-invalids unable to work again.

The presence of complications, no matter how trivial they may appear, is of serious prognostic import. Emphysema is the most common, being present in almost all cases and increasing in direct proportion to the stage of the disease. In the advanced stages, by further reducing the vital capacity, it adds to the dyspnea and cyanosis, seriously curtailing physical activity. Roentgenologic evidence of emphysema is usually readily detected and increases with the stage of the disease. Large emphysematous bullae may resemble pneumothorax; at necropsy, they were always found in the anterior portion of the lungs surrounding the massive consolidations. If emphysema is extensive, permanent improvement cannot be expected.

TABLE III

STAGE

	Improved		Died	
	Number	Per Cent	Number	Per Cent
Stage I	9	11.3	10	10
Stage II	29	37.6	32	32
Stage III	39	50.6	58	58
	77		100	

The second most common complication is tuberculosis. Gardner's[2] widely quoted estimate is that 75 per cent of all patients with advanced silicosis die of tuberculosis. While this figure may be too high for coal miners, there is, nevertheless, a high incidence of tuberculosis among them. A study made by the United States Public Health Service[3] in 1934 revealed that 20.4 per cent of the regular miners and 57.1 per cent of the rock workers over the age of fifty-five showed clinical evidence of tuberculosis. In another study one of us (M.J.S.[4]) found the incidence of tuberculosis in direct proportion to the amount of silicosis. If tuberculosis is present and the amount of dust in the lung is not great, the prognosis depends largely upon the extent and variety of the tuberculosis. In the third stage, tuberculosis is always a grave complication, and its presence increases the seriousness of an already severe condition. If there is extensive cavitation, severe hemoptysis, or marked toxemia, as evidenced by high elevation of temperature or extreme loss of weight, a fatal termination may be expected in a short time. If there is little evidence of toxemia, the patient may live for years.

The roentgen appearance of the various stages of silicosis has been frequently described. As a rule, in non-complicated silicosis, there is no significant cavitation. However, in exceptional cases, cavities varying

in diameter from 15 mm. to 3 cm. may be recognized on the roentgenograms. These cavities are apparently the result of ischemic necrosis rather than of tuberculosis, as has been proved by postmortem examinations and animal inoculation. When there is massive consolidation in the lungs, it is difficult to say whether tuberculosis is present. One point which usually favors the presence of tuberculous disease is an uneven distribution of the silicotic changes. If one lung is more involved than the other, presenting a definite asymmetry, it is in most instances an indication that tuberculosis is present, even though tubercle bacilli cannot be found in the sputum. In this series, there were cases in which more than seventy consecutive sputum examinations were negative, and yet the scrapings from the cavity at necropsy showed numerous tubercle bacilli. In some of these cases, animal inoculation was negative.

While repeated negative sputum examinations do not exclude tuberculosis, when they occur in a patient suffering from silicosis complicated by a definite clinical tuberculosis, they indicate a better prognosis so far as recovery from the tuberculosis is concerned. Forty-five (58.4 per cent) of the 77 miners discharged improved had negative sputum.

Lobar pneumonia terminates fatally more often in miners than in male adult non-miners. Three hundred and fifty-two (51 per cent) of 688 miners who developed lobar pneumonia died.[5] During the same period in the same region, 484 male adult non-miners had lobar pneumonia, they were treated at the same institutions as the miners, and only 196 (40 per cent) died. The incidence of delayed resolution is higher in those with silicosis, due possibly to the pre-existing pulmonary fibrosis. Pleural effusion and empyema occur less frequently than among non-miners, probably because of obliteration of the pleural space secondary to the silicosis. Roentgenologically, the diagnosis of lobar pneumonia in the first and second stages is not difficult; but when it takes place in the third stage of the disease, it is difficult to decide whether the roentgenographic appearance is due to silicosis, tuberculosis, or a pneumonic process. So far as the clinical course is concerned, there is no remarkable difference, though the miners have more dyspnea and cyanosis, which can be explained by the pulmonary damage produced by the silicosis.

Heart disease is another common complication in silicosis. In a study of 541 miners,[6] 126 (23.3 per cent) died of some form of heart disease, whereas among the 730 non-miners, 99 (13.5 per cent) died of heart disease. These findings were based upon the clinical as well as the necropsy studies. The most common form was chronic myocardial degeneration with hypertrophy and dilatation of the right side of the heart. Coronary arteriosclerosis, aortic aneurysm, and angina pectoris were less frequent.

The hypertrophy and dilatation of the right side of the heart is, in all probability, due to the increased intrapulmonary pressure accompanying emphysema and the extensive pulmonary vascular sclerosis, so commonly found in the third stage of silicosis. It is interesting to note that the cases of silicosis with most marked cardiac hypertrophy and dilatation were the non-tuberculous patients. In patients with complicating tuberculosis, symptoms of myocardial insufficiency are often seen, but actual hypertrophy is comparatively rare. This may be due in part to the fact that those with superimposed tuberculosis do not live long enough to develop cardiac hypertrophy. Death from cardiac failure is rare in non-silicotic pulmonary tuberculosis, but it is by no means rare in tuberculous silicosis.

As already mentioned, dyspnea is the most common symptom in silicosis. With a view to determining whether it is entirely due to emphysema or principally secondary to myocardial insufficiency, venous pressure, velocity of pulmonary circulation, and vital capacity were studied.[7] It was found that the pulmonary circulation time was prolonged in practically all the incapaci-

tated miners, the time varying between eleven and thirty seconds, depending upon the degree of right heart failure. Dyspnea was most marked in the cases with the circulation time over seventeen seconds, and, in this group, cyanosis and edema of the ankles were present. The degree of dyspnea was in direct proportion to the length of the pulmonary circulation time, but not necessarily to the reduction of the vital capacity.

In those with clinical evidences of myocardial insufficiency and the roentgen appearance of cardiac dilatation, the prognosis is hopeless. These are the patients complaining of dyspnea, cough, and expectoration, who never have fever; one may safely say that a sick miner with respiratory symptoms without fever is going to die of myocardial failure.

In a study of 507 miners,[8] we found 22 cases of spontaneous pneumothorax. Seven of these were among 198 non-tuberculous patients (3.5 per cent), whereas 14 occurred in 308 with tuberculosis (4.5 per cent). In 3 instances, the pneumothorax was bilateral. This condition may be asymptomatic or associated with severe dyspnea, pain in the chest, and be followed by pleural effusion and empyema. For the latter group, the prognosis is particularly grave.

Spontaneous pneumothorax complicating silicosis with or without tuberculosis has certain characteristic roentgenologic features. Unlike pneumothorax in non-silicotic cases, the lung is not reduced greatly in volume. There appears to be two reasons for this: first, the lung is so fibrotic and firm that collapse is impossible; second, the pleural adhesions are so numerous and extensive that the lung cannot separate from the chest wall. In the majority seen in third stage silicosis, there is only a thin film of air along the lateral aspect of the chest wall. The lower lobes usually show the greatest collapse; the semi-rigid upper lobes remain suspended in the pneumothorax cavity. The diaphragm is pushed downward, and the mediastinum is never markedly displaced. Pneumothorax has to be differentiated from bullous emphysema and pulmonary cystic disease. In pneumothorax, the lateral contour of the lung can generally be made out, and the size of the pneumothorax may change. However, such is not the case in either cysts or emphysematous blebs. In cysts and blebs, attenuated bands of pulmonary tissue may be recognized.

Although pulmonary tuberculosis is a common complication in silicosis, extrapulmonary tuberculosis, such as tuberculosis of the larynx and the intestines, appears to be less frequent than among non-miners. However, when it does occur, the prognosis becomes doubly unfavorable.

In the present study, there were 4 cases of carcinoma of the bronchus. In a condition such as silicosis, in which chronic irritation of the tracheobronchial tree is an outstanding feature, one might expect bronchial carcinoma to be a frequent complication. However, this is not the case. Although hemoptysis may occur in silicosis complicated by pulmonary tuberculosis, in pure silicosis it is rare. Repeated hemoptysis without tubercle bacilli in the sputum should arouse the suspicion of bronchial carcinoma.

SUMMARY AND CONCLUSIONS

1. In a study of 511 anthracite coal miners with silicosis, it was found that only 77 were discharged as improved, while 243 were unimproved and 191 died.

2. The ages of those who improved and those who died varied from fifteen to sixty-nine years, with the majority in the fourth, fifth and sixth decades. Most of the deaths occurred in the fifth and sixth decades in those who had worked from eighteen to twenty-three years.

3. Emphysema is the most common complication, and, when extensive, prognosis is unfavorable.

4. The second most common complication is tuberculosis. The prognosis in the first and second stages of silicosis complicated by tuberculosis is the same as in non silicotic tuberculosis; but in Stage III, the prognosis is made much worse. Patients with clinical tuberculosis but with negative

sputum have a better prognosis than those with clinical tuberculosis and positive sputum.

5. The roentgenologic changes most suggestive of tuberculosis are asymmetrical consolidation and cavitation, regardless of the findings in the sputum.

6. Lobar pneumonia terminates fatally more often in patients with silicosis than in non-silicotic patients.

7. Heart disease, which is a common accompaniment of silicosis, has a characteristic clinical course and makes the prognosis unfavorable. The most common type is myocardial degeneration.

8. Miners with clinical symptoms of myocardial disease and roentgenologic evidence of cardiac enlargement without symptoms and toxemia usually suffer cardiac deaths. Those with clinical and roentgenologic signs of heart disease but with marked toxic symptoms of tuberculosis usually die rapidly of the latter disease.

9. Spontaneous pneumothorax occurs more frequently in silicosis complicated or uncomplicated by tuberculosis than in any other pulmonary disease; it was present in 22 instances in the total series. It may be bilateral and affects the prognosis unfavorably.

10. Carcinoma of the bronchus, although not a common complication, makes the prognosis hopeless.

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THE EPIHYAL BONE

A CONSIDERATION OF SOME SMALL ACCESSORY BONES OF THE NECK

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THE following case brought to our attention the presence and significance of epihyal bones.

The patient (P. McCl., Harper Hospital No. 159275) was a factory worker, aged thirty-three. For eleven months his complaints had been a feeling of constriction in the throat with a periodic sense of obstruction and difficulty in breathing particularly at night. He complained of much pain in the epigastrium associated with belching and pyrosis and also of constipation, weakness, loss of weight, and nervousness. In the family history it was learned that one brother had died of a growth in the larynx.

The physical examination was essentially negative except that some excessive lymphoid tissue and evidence of chronic inflammation were seen at the base of the tongue during the laryngoscopic study. The question of some neuromuscular incoördination in the throat and of esophageal diverticulum was raised and gastrointestinal roentgen examination advised.

Laboratory examination of the blood, urine, spinal fluid, and gastric juice revealed nothing abnormal.

The roentgen studies, including examination of the chest, gastrointestinal tract and neck, were negative except for the presence of large epihyal bones observed in the lateral study of the neck (Fig. 1). From the character and multiplicity of the patient's complaints, it was believed that they played no causative rôle and they were therefore regarded as an incidental finding of no clinical significance.

FIG. 1. Lateral roentgenogram of the neck showing two large epihyal bones between the angles of the mandible and the body of the hyoid bone.

The finding of these epihyal bones prompted us to look more carefully for accessory bones in the neck and finally to study a group of 500 unselected cases. The material consisted for the most part of roentgen studies of the skull which included the upper neck area. This provided stereoscopic films in both lateral projections for examination. A few of the films were from routine studies of the cervical spine, but in general these did not prove as satisfactory as the skull roentgenograms.

For each case a notation was made regarding the presence of the epihyal bone and its length, the appearance of the styloid process and whether a separate center of ossification was present, and the appearance of the hyoid bone with particular attention to the greater and lesser cornua. The usual position of these structures is shown in Figure 2.

In the early months of intra-uterine life the hyoid bone is represented by hyaline cartilage which is directly continuous with the styloid process of the temporal bone. Ossification occurs from six centers. The two which give rise to the lateral parts of the body (basihyal) and the two centers for the greater cornua (thyrohyals) are de-

rived from the third branchial arch and appear at birth or shortly before. The two centers for the lesser cornua (ceratohyals) are derived from the second branchial arch and appear later and more variably. The second branchial arch also gives rise to the stylohyoid ligament and the styloid process of the temporal bone.

In about 50 per cent of our cases there was no osseous union between the corpus and greater cornua of the hyoid bone and the actual incidence was thought to be probably somewhat higher. The lesser cornu is not constantly demonstrable and was evident in only about 20 per cent of the cases studied. In more than half of these it was separated from the corpus by cartilage. According to Parsons there is a true diarthrodial joint present which disappears only in old age. The lesser cornua are the points of attachment for the stylohyoid ligaments.

The stylohyoid ligament rarely ossifies and when it does so the structure is called the epihyal bone. When the bone is small in size and occurs near the hyoid bone it may be confused with the lesser cornu. However, the lesser cornu is usually only a few millimeters in length, but may be 10 to 12 mm. (Cunningham). In the 500 cases studied, we found an epihyal bone measuring 10 mm. or more in length on the film in 30 cases, giving an incidence of about 6 per cent. According to Gray, the bone is present more constantly in some of the lower animals. In 2 of our cases the bone was very prominent on both sides and measured 5 cm. in length on the film. No correlation of the appearance or size with age or sex was demonstrable. Most of the patients were examined for an injury to the skull and none gave a complaint referable to the neck.

When the epihyal bone occurs near the styloid process of the temporal bone it may be confused with a separate center of ossification for the tip of styloid process. The styloid process is very variable in length. In about 25 per cent of the cases it could not be demonstrated on the roentgenograms and in about 10 per cent it extended to the level of the angle of the mandible. The ossification of the styloid process occurs from two centers, the tympanohyal which appears before birth and soon unites with the temporal bone, and the stylohyal which is said to appear in the second year of life and later becomes united with the tympanohyal. Rarely this union does not occur; this circumstance was recognized in about 3 per cent of our series.

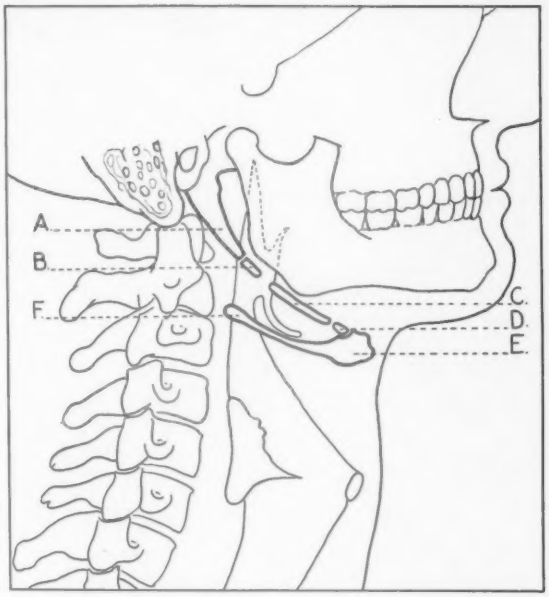

Fig. 2. Diagrammatic sketch showing positions of some accessory bones. *A*, styloid process of the temporal bone; *B*, separate center of ossification for the tip of the styloid process; *C*, epihyal bone; *D*, lesser cornu of the hyoid bone; *E*, corpus of the hyoid bone; *F*, greater cornu of the hyoid bone.

The small bones in the upper part of the neck are seen frequently by the roentgenologist and he should be familiar with their presence and the variations in their appearance. Even when large in size they are probably never productive of symptoms. Occasionally they may be mistaken for foreign bodies.

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LEIOMYOSARCOMA OF THE FUNDUS OF THE STOMACH WITH PERFORATION*

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ALTHOUGH the literature contains numerous reports of myogenic sarcoma of the stomach, it continues to be rarely seen by individual clinicians and pathologists. Chaffin,[3] in 1938, collected 363 cases of leiomyosarcoma of the stomach and added his own case. Since then single cases have been reported by Wagner,[6] Belitskiy,[2] Jordan,[4] and Baumgartner,[1] bringing the total up to 368 authentic cases.

The incidence of sarcoma to other malignant lesions of the stomach in our material is 1.5 per cent. In a series of 12,450 consecutive necropsies performed at the Cook County Hospital from 1929 to July, 1939, inclusive, 3 cases of leiomyosarcoma of the stomach were encountered. The presence of these tumors on the anterior wall, together with a completely misleading clinical course, serves to strengthen the contention that a diagnosis of sarcoma of the stomach is extremely difficult.

It is not within the province of this report to discuss the already voluminous literature. Any contribution that may elucidate its obscure diagnostic features is worthy of record. Accordingly the following case is presented.

CASE REPORT

L.F., colored female, aged forty-one, was first admitted to a medical ward of the Cook County Hospital on October 8, 1937, with a complaint of pain in the left lower chest of about eleven days' duration. This was associated with fever, cough, expectoration of mucus, and night sweats. There had been a 20 pound weight loss in the past year with some dyspnea and occasional periods of nausea and anorexia. The gastrointestinal history was essentially negative.

Physical Examination. Temperature 103° F., pulse 120, respirations 24, blood pressure 115 systolic, 55 diastolic; resting comfortably. There was limited chest expansion on the left side. The abdomen was slightly distended and tenderness was elicited in the left hypochondrium. A left lower lobe pleuropneumonic process was diagnosed. However, films of the chest revealed only an accentuation of the bronchovascular arborizations. An early hematogenous dissemination from some tuberculous focus was considered. Repeated sputum examinations were negative. Although she presented a picture of sepsis at the outset, there was gradual improvement and she was discharged ten weeks later.

She returned on February 18, 1938, about two months after her discharge, with complaints of pain in the left lumbar region and malaise; temperature was 99.2° F. She did not appear acutely ill.

Examination at this time revealed some tenderness in the upper abdomen and a palpable mass in the epigastrium. The conjunctivae were pale. The red blood cell count was 3,100,000 and the white blood cell count 7,700; hemoglobin 42 per cent. A chest roentgenogram at this time reported a marked elevation of the left dome of the diaphragm, and roentgenoscopy was advised to rule out subphrenic abscess. On February 24, patient first began vomiting. An analysis of the gastric contents showed no free acid. Stool examination was repeatedly positive for occult blood.

On March 3, a barium study of the stomach revealed a constant defect in the pars cardia with downward depression and flattening suggestive of an intrinsic lesion (Fig. 1). A re-check on March 18 confirmed the previous findings and a diagnosis of carcinoma of the cardia of the stomach was made. At this time patient began running a high temperature and the white count showed 23,000 cells.

The patient was now acutely ill and very toxic. The liver and epigastric mass were very tender. Perforation of the stomach was suspected. The patient's condition grew rapidly worse and she died about six months after the first admission and about one year after onset of symptoms.

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Essential Autopsy Findings (Performed by J. D. Kirshbaum). The body was that of a well developed and well nourished colored female. On opening the abdomen, the liver was found to be somewhat enlarged. The intestinal loops were covered by flakes of fibrin. There was about 200 cc. of a foul smelling, purulent, yellowish-green material in the abdominal cavity. The mucosa of the stomach was covered by a small amount of bloody mucoid material.

Fig. 1. Roentgenogram of the stomach shows a defect in the pars cardia with downward depression and flattening.

In the region of the fundus, on the anterior surface 6 cm. from the cardiac orifice, there was a fungating tumor mass 9×8×3 cm. (Fig. 2). The periphery was firm, the central portion partially necrotic containing a cavity 3 cm. in diameter. This cavity communicated with another, 9×6 cm., which was partially located within the left lobe of the liver. The perigastric lymph nodes were enlarged forming masses up to 10×6 cm. which on sectioning were yellowish-gray, medullary, and contained several large central cavities communicating with the larger cavity described above. The left lobe of

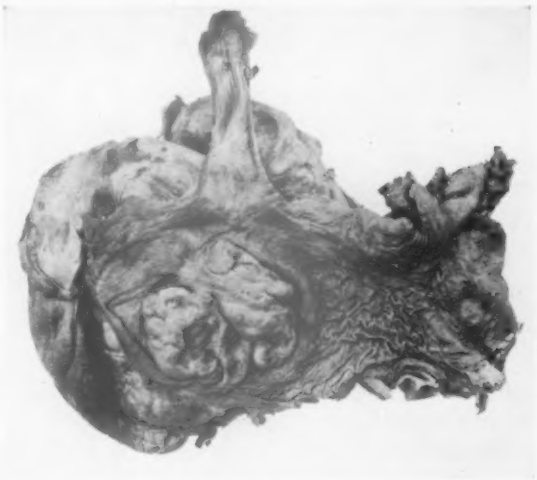

Fig. 2. Photograph of the stomach showing the tumor centrally ulcerated. Note fixation of the stomach to the liver.

the liver was, for the most part, transformed into tumor tissue which fused with the enlarged lymph nodes.

Microscopic study of the tumor in the stomach revealed it to be made up of interlacing bundles of elongated cells, containing regular

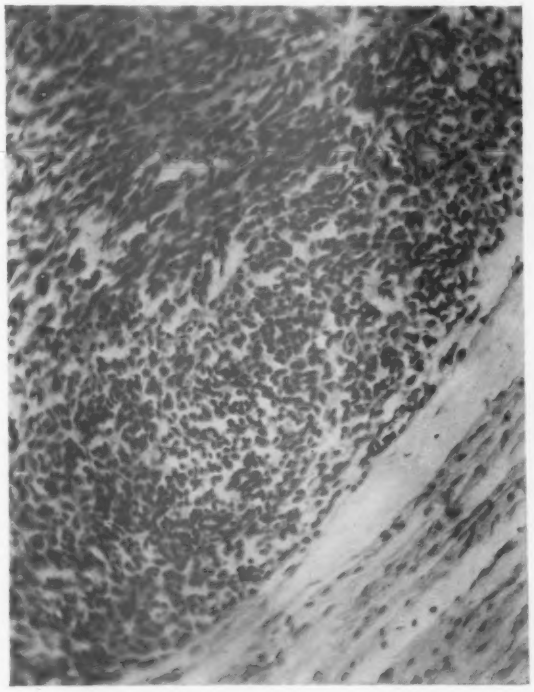

Fig. 3. Photomicrograph of the tumor of the stomach. Note the benign character of cells (hemalum-eosin, ×300).

spindle shaped nuclei with rounded poles (Fig. 3). Only an occasional atypical mitotic figure was seen. The outer layer of the muscularis propria was almost completely replaced by densely packed tumor cells. There was a marked infiltration with round cells and large mononuclears in the adjacent portions.

Anatomic Diagnosis. Ulcerated leiomyosarcoma of the anterior wall of the fundus of the stomach; extension of the tumor into the left lobe of the liver with ulceration and perforation into the peritoneal cavity; extensive metastases to the perigastric lymph nodes; diffuse suppurative peritonitis; compression atelectasis of the left lower lobe of the lung with elevation of the left dome of the diaphragm; fibrinous pleuritis on the left side.

DISCUSSION

This case serves to emphasize the great difficulties encountered in arriving at a diagnosis of sarcoma of the stomach. In fact, the true nature of the condition was not even suspected. Knowing as we do that sarcoma offers a somewhat better prognosis as to operability and duration of life, a constant attempt at differentiation from carcinoma should be made.

This instance also brings to point the rather misleading histological descriptions of these tumors. It was only with great difficulty that a few atypical mitotic figures could be found. In fact, no portion of the tumor could really be called malignant, suggesting that we may here be dealing with the so-called metastasizing leiomyoma of the stomach. Indeed, pathologically this case is practically identical to that described by Melnick[5] in which he emphasized the unmistakably benign character of these tumors. In our case, there was no evidence of metastasis to the liver, but rather an extension with a sharply defined zone between the tumor and liver parenchyma, the latter being markedly compressed.

SUMMARY

A case of leiomyosarcoma of the stomach is presented with a discussion of its histological character, drawing attention to its close similarity to the rare benign metastasizing leiomyomas described in the literature.

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PERSISTENCE OF THE NOTOCHORD*

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OF THE numerous anomalies of the vertebral column, the defect caused by persistence of the notochord has received the least attention in the literature.

The notochord (chorda dorsalis), or primitive backbone, is derived from the undifferentiated tissue of the blastopore, where the ectoderm and the entoderm meet, and is probably mesodermal in origin.[1] In the embryo it lies just ventral to the neural streak and just dorsal to the primitive gut. As the head segment grows, the notochord recedes caudally and becomes enclosed in the vertebrae.

Soon after the appearance of the notochord, sclerotomes are formed in the undifferentiated tissue which lies dorso-lateral to it. These sclerotomes migrate to a position just lateral to the notochord and separate into a dense caudal and a less dense cranial part. This dense caudal portion of each sclerotome unites with the less dense cranial portion of the sclerotome just below it to form one lateral half of a vertebral body. These paired lateral half-vertebrae fuse with each other, anteriorly and posteriorly to the notochordal canal and compress it. The notochord subsequently undergoes atrophy within the vertebral bodies, and in the adult human remains only as the nucleus pulposus of the intervertebral discs.

Joplin,[6] in a review of the development, physiology and pathology of the intervertebral disc, showed a section through a 14.1 mm. human embryo, six weeks old (Fig. 1). The position of the notochord and its relation to the development of the vertebral bodies are clearly demonstrated.

It can readily be seen from Figure 1 that any deformity due to the persistence of the notochord and (or) its canal would appear as a defect more or less centrally located in the bodies of the vertebrae. Despite an intensive search through the available literature only a few cases with such a deformity were found.

The first case is credited to Musgrove,[7] who in 1891, while doing routine sections of vertebral columns in the dissecting rooms at Edinburgh, encountered a core of unossified tissue in the center of the fourth lumbar vertebra of a young adult male. This tissue extended from the superior to the inferior surface of the body and was continuous with the intervertebral discs above and below. The adjacent vertebrae were normal and the intervertebral spaces were preserved. This defect measured 12 × 15 mm. in cross section and could not be detected on external examination of the anatomical specimen. Microscopically it was seen to be composed of essentially the same type of tissue usually found in the intervertebral discs.

Schmorl[9] discussed the rôle of the notochord in the development and maldevelopment of the vertebral column, and reported 2 cases discovered at autopsy, together with roentgenograms of the anatomical specimens. Both of these patients were young adults who had died of unrelated causes. In each of them only a single lower dorsal vertebra was involved, and in both of them the notochordal tissue passed through the body of the vertebra and was continuous with the adjacent intervertebral discs. The photographs of Schmorl's specimens are almost identical in appearance with Musgrove's illustration, and his roentgenograms strikingly resemble those of the case reported at this time. In addition, these same authors mention 3 other similar cases.[4,5] One of these cases[4] was proved at necropsy. One other was credited to Blount, but had not been previously published. Since the appearance of Schmorl's monograph, this patient has died and autopsy was performed. The postmortem findings confirmed the

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roentgenologic diagnosis of persistent notochord.[2]

Herniations of the intervertebral discs into the bodies of the vertebrae were first described by Schmorl[8] and are now generally known as "Schmorl's nodes." Ferguson,[3] in discussing these nodes, stated that they occurred in childhood and became more pronounced as the vertebrae increased in size, but thought that they were of no clinical significance. Schmorl, however, believed that these nodes indicated a structural weakness of the vertebrae, and that heavy labor and strenuous exercise should be forbidden when they are present.

In 1928 Schmorl[8] found these nodes to be present in one or more vertebrae in 35.6 per cent of 1,160 autopsies. When his figures were broken down by decades, it was noted that there was no increase in the occurrence of these nodes until the eighth and ninth decades. The fact that there were approximately as many of these defects found in the early decades as there were in the decades of middle life indicated that at least a good proportion of them were due to congenital malformations. The increase in the very late decades would indicate that the degenerative processes played a rôle in the development of some of them. He and Junghanns[9] discussed the possible causes of these herniations into the vertebral bodies. These I have tabulated:

I. Developmental abnormalities
   Failure of the notochordal canal to close completely, leaving a defect in the bone adjacent to the nucleus pulposus.

II. Degenerative changes
   Arthritis
   Osteoporosis

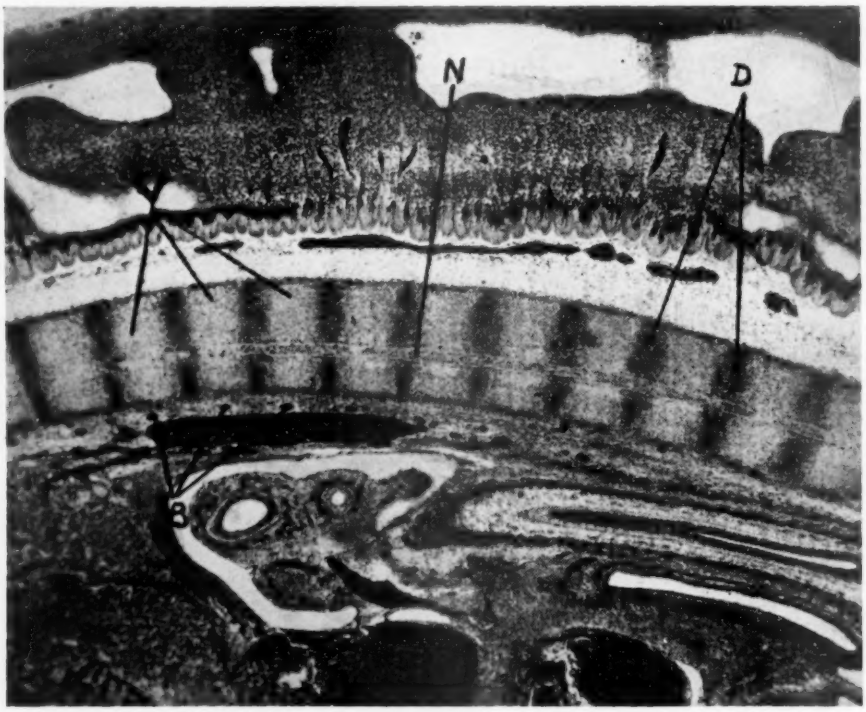

Fig. 1. Second to ninth thoracic vertebral region in an embryo 14.1 mm. long, six weeks old. The notochord, *N*, is seen passing through the segmented masses of cells. Above is dorsal, below is ventral where cross-sectioned blood vessels, *B*, may be seen opposite the lighter areas, *V*, which form the vertebral bodies; the darker areas, *D*, form the discs. (After Joplin, courtesy *Surg., Gynec. & Obst.*)

III. Inflammation
Tuberculous
Nonspecific
IV. Neoplasm
Which may cause bone destruction adjacent to the disc into which the uninvolved disc may protrude.
V. Trauma
A break in the cortex may occur, sometimes at the site of a congenital defect, of the type mentioned under I.

The similarity between the less deformed vertebrae in the case here reported and the appearance of the well-known Schmorl node is quite striking. This case is the only one of its kind in the records of Cleveland City Hospital, and offers further evidence of the relationship between persistence of the notochord and Schmorl's nodes.

Fig. 2. Full-length photograph of the patient taken in April, 1939. Note the extensive skin involvement, most marked on the extremities and the face. The deformities of the arms and legs due to contractures can be seen. (The patient was unable to stand alone without leaning against the wall.)

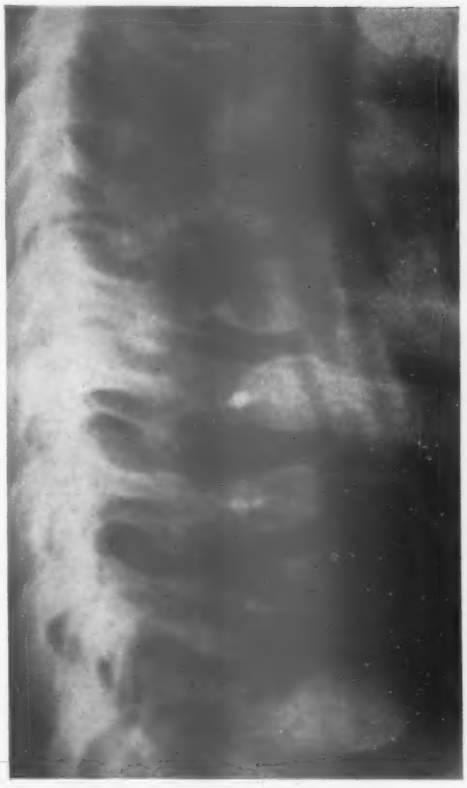

Fig. 3. Lateral view of the dorsal spine taken on April 1, 1933. Note the indentation of the superior and inferior surfaces of all the vertebrae, varying in extent. The fourth dorsal vertebra is completely divided, the sixth, seventh and ninth almost completely severed.

REPORT OF CASE

A. S., male, aged nineteen, of Hungarian parentage, was admitted to the dermatological service of City Hospital on January 24, 1939. Hospital records revealed that this patient has been followed on the wards and in the out patient departments of City Hospital and Lakeside Hospital since the age of nineteen months. At that time, in December, 1920, he was admitted to Lakeside Hospital for the treatment of a chronically inflamed, red, thickened and scaly skin, which had first appeared following pneumonia at the age of six months. His delivery had been normal, he had received adequate nutrition, and was apparently a normal infant up to the age of six months. Treatment failed to improve the condition of the skin. Four months later he developed diphtheria and was admitted to the contagious division of City Hospital. On a subsequent admission, in 1924,

Fig. 4. Lateral view of the lumbar spine taken on April 1, 1933. The indentations are not as deep as those seen in the dorsal vertebrae, but through the body of the third and fourth lumbar vertebrae there can be seen a line of increased density, representing bone condensation around the site of the notochord, and continuous with the indentations on the surfaces.

again for the same unimproved skin lesions, a diagnosis of congenital ichthyosiform erythroderma was made. It was not until 1933, when the patient was almost fourteen years old, that the first roentgenograms were made, primarily because he was considerably under the normal height for his age. He weighed 46 pounds and had a mental age of nine and a half years at that time. His height was not recorded because he was unable to stand on account of the formation of contractures of the hands, feet, elbows and knees, which were thought to be secondary to the long standing chronic inflammation of the skin.

Biopsy of the skin taken at Lakeside Hospital just prior to the present admission was reported as consistent with the clinical diagnosis of congenital ichthyosiform erythroderma. He was then referred to City Hospital for further therapy for his skin lesions.

Physical examination revealed a small, thin, white boy, 49 inches tall, who weighed 61 pounds. The contractures noted on the previous admissions were still present, but were less troublesome at this time, and the patient was able, with some difficulty, to stand alone. The skin over the face and extremities was thickened and scaly. On the anterior surface of the legs there was a heaping up of the skin to a thickness of more than 1 cm. The trunk showed little involvement. The heart and lungs were normal. Visual fields were normal. The Wassermann and Kline tests were negative. Tuberculin test 1/10,000 was positive. Other laboratory findings were not abnormal. Intelligence tests yielded an I.Q. of 91.

Roentgen Findings.

January 25, 1933. Lateral view of the sella turcica showed it to measure 7 mm. by 6 mm.

March 31 and April 1, 1933. Anteroposterior

Fig. 5. Lateral view of the dorsal spine taken March 11, 1939. There is very little change in the intervening period of six years. The epiphyseal plates have appeared. The intervertebral spaces are preserved. The height of each vertebral body at the anterior edge is the same as the rest of the body, indicating that no wedging has taken place.

and lateral views of the lumbar and dorsal spine showed an indentation of the superior and inferior surfaces of all the vertebrae. This indentation was most pronounced from the second to the tenth dorsal vertebrae, the third and fourth bodies, as seen in the lateral view, being completely severed. In those bodies in which the separation was not complete, there could be seen a line of increased density in the longitudinal axis of the vertebrae. surrounding this defect. The margins of those bodies which had not been completely perforated were preserved, the defect occurring in the center of the upper and lower surfaces, i.e., at the site of the notochord. The appearance was not that of bone destruction, but rather absence of bone. The intervertebral spaces were preserved (Figs. 3 and 4).

January 27 and March 11, 1939 (Present Admission). Anteroposterior and lateral views of the entire spine again showed the previously described defects. The epiphyseal plates of the vertebrae have appeared, but have not united with the bodies. The changes were least marked in the cervical region, and throughout the length of the entire spine were best seen in the lateral views (Figs. 5, 6 and 7).

Fig. 6. Lateral view of the lumbar spine taken January 27, 1939. Note the cupped indentation on the upper surface of the first lumbar vertebra, and the opposing indentation on the adjacent surfaces of the other lumbar vertebrae. The cupping between the first and second lumbar vertebrae is characteristic of a Schmorl node.

Fig. 7. Anteroposterior view of the dorsal spine taken January 27, 1939. The deformity cannot be diagnosed with certainty in this projection. There is a narrow cleft in the center of the superior surface of the third dorsal vertebra.

April 1, 1933 and February 20, 1939. Posteroanterior views of both hands showed considerable distortion of the epiphyses and atrophy of the terminal phalanges. There was a thickening and wrinkling of the skin, which cast a shadow of unusual density. There was marked onychogryphosis. The epiphyses had failed to unite at the usual time. Comparison with Todd's[10] standards for skeletal maturation revealed that at the age of thirteen years and ten months the hands had reached a level of skeletal development usually seen at eleven years. At the age of nineteen years and nine months, the stage of development was only fourteen years and three months (Fig. 8). This indicated a severe retardation.

April 3, 1939. Posteroanterior view of the

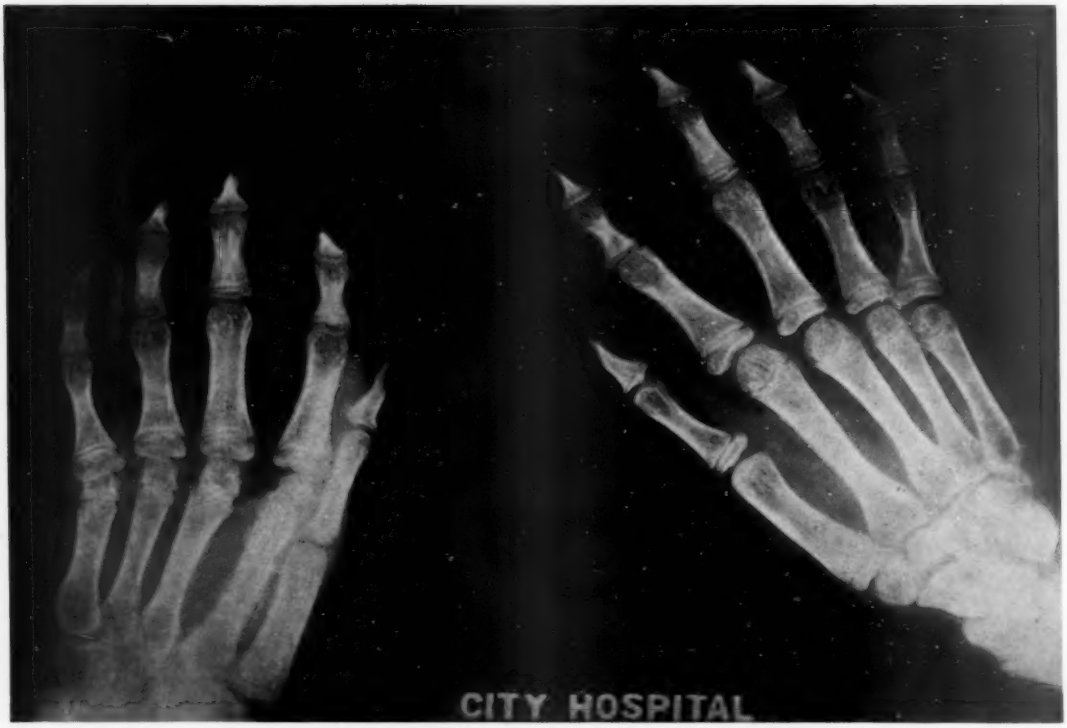

Fig. 8. Posteroanterior view of both hands taken February 30, 1939, shows an atrophy of the terminal phalanges, a thickening of the skin and onychogryphosis. Note the increased density of the skin shadow. Most of the epiphyses are as yet not united to the diaphyses although the patient is almost twenty years old.

chest showed a streaked mottling, extending laterally into the right lung field from the right hilum. In the lateral view this infiltration was seen to be in the middle lobe. There was a small amount of calcification in both hila. These findings were interpreted as representing pulmonary tuberculosis, probably a spread from a primary infection.

Course. Therapy to the skin lesion was of no help. Following the film of the chest on April 3, 1939, the patient was transferred to the Lowman Tuberculosis Pavilion of City Hospital. Serial films showed a slow, but progressive, fibrosis of the lesion in the right lung, and on August 12, 1939, he was sent home to rest, with a good prognosis for cure of his tuberculosis.

COMMENT

In the differential diagnosis, the absence of clinical and roentgenologic evidence of trauma, infection, osteoporosis, or of new bone formation, and the absence of any symptoms related to the back, led to the conclusion that these changes in the bones represented a congenital defect of the vertebral column. The history of shortened stature since infancy further favored this conclusion.

The central location in the vertebral bodies, the extent of the process, and the similarity in appearance of the defects to the proved cases reported, led to the diagnosis of persistence of the notochord.

Since it is reasonable to assume that the same factors were responsible for the defect along the entire length of the spine, and since the resemblance between the less involved vertebrae and Schmorl's nodes is so striking, it is probable that the complete separation of some of the vertebrae represents only a further stage of the same process. In some of the vertebrae the notochord has apparently atrophied completely, leaving only a small defect at the surface, and in others it traverses the whole vertebral body.

SUMMARY

1. The available literature has been reviewed and only five proved cases of persistence of the notochord have been found. One other probable case has been reported.

2. The embryological development and fate of the notochord has been reviewed.

3. The similarity of the defects known as Schmorl's nodes, and those due to the persistence of the notochord has been noted. The conclusion is drawn that these conditions are related, and this case is offered as further evidence that at least some of the cases of Schmorl's nodes are congenital in origin.

4. A case is reported showing this defect throughout the length of the dorsolumbar spine. No previously reported case involves so many vertebrae. In addition, this patient presents evidence of retardation of skeletal growth, and a long standing chronic skin disease which is regarded as congenital in origin.

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FRACTURES OF THE SPINE AFTER METRAZOL CONVULSIVE THERAPY AND OTHER CONVULSIVE STATES*

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PURPOSE

SINCE the benefits of pharmacological shock therapy in the treatment of the psychoses have included many thousands of individuals, any form of complication constitutes an important consideration for all branches of medical practice. Meduna and Friedman[4] summarized the results of metrazol treatment in 2,937 cases in the United States and Europe, listing the percentage of complications as 2.2 in this large series, and enumerating as the important complications the following: dislocations of the jaw, fractures and dislocations of the joints in the extremities, exacerbation of inflammatory processes, and acute pulmonary and myocardial failures.

Stalker[9] in November, 1938, was the first to call attention to the vertebral compression fracture which may follow convulsive therapy. Polatin and his coworkers[6] have reported the presence of this more constant complication in 22 cases out of 51, an incidence of 43.1 per cent. Bennett and Fitzpatrick,[1] and Hamsa and Bennett[2] have corroborated the above findings and suggested various means of prevention.

The purpose of this study is to discuss the roentgenographic description of these spinal fractures observed in a series of 32 cases treated with metrazol in the Psychiatric Division of the Philadelphia General Hospital. We shall also attempt to interpret the possible method of production and compare the findings with those seen after other convulsive states, such as tetanus, epilepsy, meningovascular syphilis and insulin hypoglycemia.

ORGANIZATION OF THE STUDY

Thirty-two metrazol cases were selected at random for roentgen study, including some who were being treated just prior to roentgen examination, and others who were attending our follow-up neuropsychiatric clinic. The entire spine was examined, taking anteroposterior and lateral views. Roentgenograms were taken before and after treatment in 5 cases to prove the relationship between the convulsions and the fractures. Seven cases with reported fractures were also examined clinically by Dr. John Royal Moore of the Orthopedic Department. After the occurrence of convulsions, roentgenograms were taken of the spines of 3 patients receiving insulin hypoglycemic therapy, 3 epileptics, and 1 patient with meningovascular syphilis.

IMPORTANT FINDINGS

Roentgen examination revealed the presence of a vertebral fracture in 14 metrazol cases out of 32, or 43.9 per cent, with 2 more as questionable. In the ordinary types of fracture of the spine, the location is usually in the twelfth dorsal, first and second lumbar vertebrae, or fourth and fifth cervical vertebrae. There are two main types of fractures, first the comminuted in which the body is crushed and deformed, the result of a very severe trauma; second, compression fractures where there is a collapse of a portion of the body, the deformity varying from a slight depression in the anterior or lateral margin, to a wedge-shaped deformity. There is another condition in the spine described as Kümmell's disease where there are no bony changes immediately after the injury, but a collapse of the vertebrae after several weeks or months have elapsed. It is supposed to be a non-tuberculous osteitis, the result of injury, and the changes are not apparent until the process of repair has removed the

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damaged but supporting trabeculae. Kümmell's disease usually involves a single body and occurs in the mid and lower dorsal regions.

In this metrazol series, except for a few cases, the dorsal vertebrae from the fourth to the seventh were involved. More than one vertebrae were fractured, and although the deformity is not unlike that seen in Kümmell's disease, the multiplicity of the fractures and their location would be against the fracture occurring in Kümmell's disease.

The roentgen findings were:

(1) Loss of normal concavity of the anterior or upper articulating surfaces of the body of the vertebrae.

(2) Zone of increased density at or below the articulating margin of the vertebrae.

(3) Lateral or anterior wedging of the vertebrae.

(4) Fragmentation, sclerosis and saucerization of the articulating surfaces.

(5) Flattening and shortening of the body vertically, with elongation transversely.

(6) Narrowing of the discs and spur formations.

(7) Involvement mainly of the upper articulating surfaces of the body.

The more recent fractures showed flattening, rarefaction and loss of normal contour. When healing took place, fragmentation, sclerosis, wedging and arthritic changes were the more common findings. In the study of the remaining vertebrae, there was no evidence of decalcification, rarefaction or any other abnormal appearance to suggest interference with calcium or phosphorus metabolism.

Fig. 1. Case 1. Slight depression and sclerosis of upper articulating margins of fourth, fifth and sixth dorsal vertebrae, with narrowing of the discs.

STATISTICAL TABULATED STUDY

Table 1 summarizes the important considerations in the clinical evaluation of these patients. After a study of this table it will be noted that 14 cases with very definite fractures were visualized; in addition, there were 2 questionable alterations in the normal bony contours. The ages of the patients with fracture ranged between eighteen and fifty-two years with 4 patients above the age of forty. The patients without fracture fell between the ages of twenty and forty-eight years, with 2 patients over forty years. Six to twenty convulsions constituted the course of therapy in the patients with fracture, while those without fracture were subjected to from three to twenty treatments. About the same number of patients had complaints of back pain among the groups with and without roentgenographically demonstrable alterations. Dr. John Royal Moore could find but one patient (No. 2, W.W.) with objective evidence of spinal column injury, consisting of a very definite kyphos in the upper dorsal region. In an attempt to evaluate the relationship among the presence of fractures, the total amount of metrazol used, the highest single dose of the drug, and the frequency of repeated doses on single treatment days, no absolute correlation could be found. In contrast to Polatin's finding, more men suffered with this complication than women. It will also be ob-

TABLE I

Case	Patient	Age	Diagnosis	Fracture	No. of Rx	Highest Single Dose (gm.)
1	W.Y.	43	M-D(D)	$D_4, 5, 6$	13	0.9
2	W.W.	24	D-P	$C_5, D_3, 6, 7$	20	0.6
3	M.M.	24	D-P	$D_4, 5, 6$	18	0.8
4	L.D.	22	D-P	$D_4, 5, 6$	19	0.9
5	J.M.	32	D-P	$D_5, 6, 7$	20	1.1
6	J.B.	49	M-D(D)	$D_4, 5, 6, L_3$	10	1.0
7	H.L.	23	D-P	D_3	15	1.3
8	E.W.	52	M-D(D)	$D_7, 8$	20	1.1
9	D.V.	31	D-P	$D_5(?)$	5	0.6
10	R.S.	18	D-P	$D_4(?)$	20	0.9
11	F.B.	27	D-P	Negative	10	0.4
12	S.P.	25	D-P	Negative	12	0.6
13	A.Z.	26	D-P	Negative	20	1.0
14	E.M.	20	D-P	Negative	20	0.9
15	A.M.	46	M-D(D)	$D_4, 5, 7$	12	0.9
16	M.P.	19	M-D(M)	Negative	20	0.9
17	O.S.	25	D-P	Negative	20	0.6
18	A.P.	24	D-P	Negative	19	0.9
19	M.R.	23	D-P	Negative	20	0.6
20	O.D.	48	M-D(D)	Negative	9	0.7
21	E.W.	27	D-P	Negative	15	0.6
22	E.M.	32	M-D(D)	$D8, 9, 10, 11, 12$	13	0.8
23	J.D.	38	M-D(D)	$D_4, 6$	10	0.6
*24	A.L.	30	D-P	$D_3, 4, 5, 6, 7$	20	1.1
25	S.T.	33	D-P	D_9	6	0.7
*26	J.K.	42	M-D(D)	Negative	12	0.6
27	P.K.	25	D-P	Negative	15	0.8
28	H.B.	40	M-D(D)	Negative	3	0.4
29	F.T.	20	M-D(M)	Negative	15	0.9
*30	E.P.	22	D-P	$D_3, 4, 5$	13	0.7
*31	F.S.	38	M-D(D)	Negative	15	0.7
*32	A.M.	35	M-D(D)	Negative	10	0.8

M-D(D)—manic depressive psychosis, depressed phase.
M-D(M)—manic depressive psychosis, manic phase.
D-P—dementia praecox.
*—roentgenograms before and after treatment.

served that 3 of the 5 patients with normal roentgenograms before treatment showed definite fractures after the convulsions.

MECHANISM OF THIS COMPLICATION

There are two possible answers to the question of the exact mechanism of this important finding: (1) metabolic factors; (2) mechanical factors.

The metabolic factors present a difficult problem to evaluate properly. Moffat[5] has shown how easily compression fractures and spinal curvatures may be produced in cases of nutritional calcium deficiency as a likely cause for the post-tetanic spinal deformity. The very great likelihood of avitaminosis among psychotic patients with poor eating habits is not to be overlooked. Another question has been raised concerning the specific action of metrazol itself in producing this complication. We are unprepared at present to answer these possibilities.

Notwithstanding the above, the balance of proof appears to be with the mechanical factors. The frequency of occurrence of this unusual type of fracture in a relatively rare

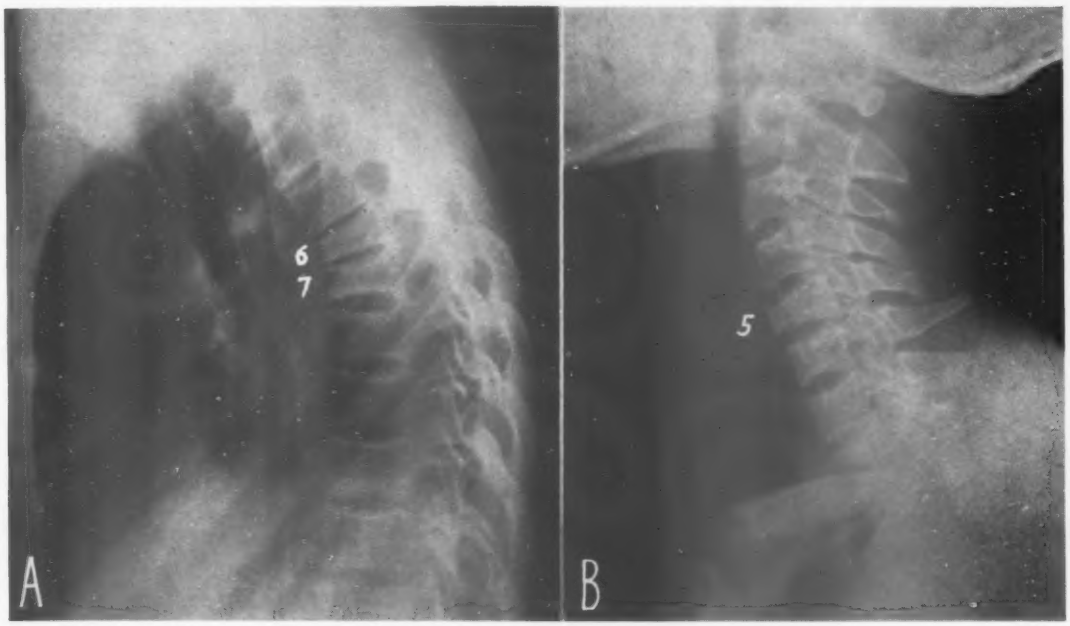

Fig. 2. Case 2. *A*, wedging and sclerosis of sixth and seventh dorsal vertebrae. Narrowing of intervertebral discs, and arthritic changes. Only minor depression of upper surface of the third. *B*, comminuted fracture of fifth cervical vertebra involving mainly the anterior half of the body and upper articulating surface.

site with such a close resemblance to the post-tetanic gibbus formation, similar as tetanus is to the convulsive episodes of metrazol therapy, points toward a mechanical break in the site of greatest vulnerability. Roberg[8] emphasizes the relative rôles of the spinal extensors and flexors, stressing the upper thoracic vertebrae as least covered by spinal erectors, so that

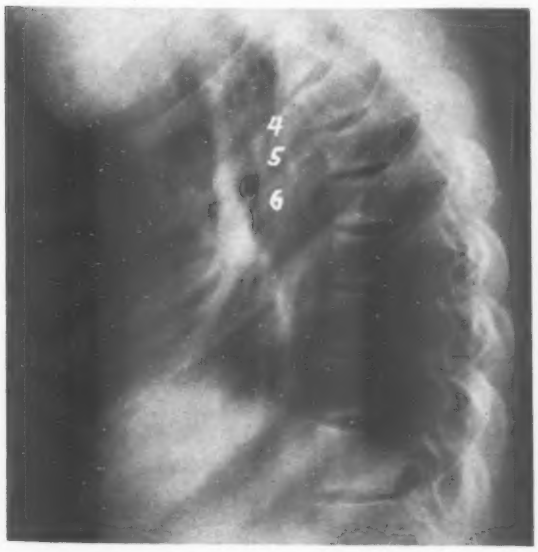

Fig. 3. Case 3. Wedging, flattening, and compression of fourth, fifth, and sixth dorsal vertebrae. Sclerosis of upper articulating margins, indentation in the anterior margins.

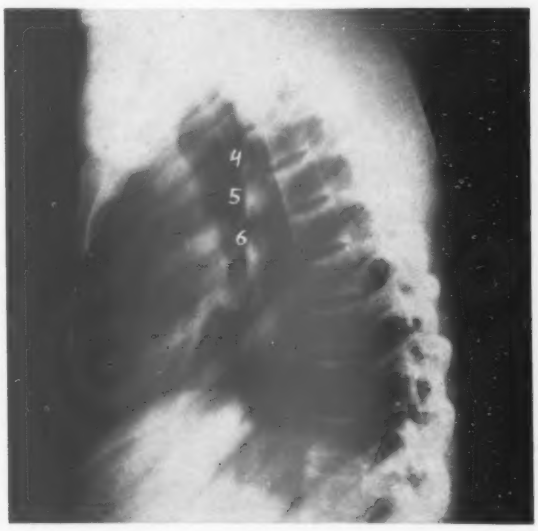

Fig. 4. Case 4. Sclerosis and saucerization of upper articulating surfaces of fourth, fifth and sixth dorsal vertebrae, with very little compression of the bodies.

Fig. 5. Case 5. Recent compression of bodies of fifth, sixth and seventh dorsal vertebrae. Very little sclerosis. Narrowing of discs, and indentation of the anterior margins.

there is a site of least resistance to a sudden contracture by the anterior trunk musculature. The upper dorsal spine is also the least flexible of all the parts of the bony column.

Fig. 6. Case 6. Flattening, elongation, and compression of fourth, fifth, and sixth dorsal vertebrae, with narrowing of the discs, and biconcave appearance of the upper articulating surfaces.

With these facts in mind in an attempt to prevent this complication, we have treated 2 patients in the position of hyperextension with a sandbag under the shoulders; during the convulsion the shoulders and legs were held down firmly in order to prevent the sudden forward flexion of the trunk. No fractures have been seen thus far in these 2 cases.

COMPARISON WITH OTHER CONVULSIVE STATES

In 1907, Lehndorff[3] was the first to report fractures resulting from the muscular contractions associated with tetanus. Roberg[8] and Rand[7] reviewed the literature, emphasizing the relationship between tetanus and juvenile kyphosis with the occurrence of the spinal deformity in the mid dorsal region. The roentgen description of the changes in the fractured vertebrae are practically identical with that seen after metrazol convulsions.

Fig. 7. Case 8. Flattening, compression of seventh and eighth dorsal vertebrae, with sclerosis of upper margins and arthritic changes in anterior margins.

During the hypoglycemic state of insulin shock therapy in the treatment of the psychoses, the occurrence of typical grand mal is not uncommon. The entire spine of 3

patients who had reacted with convulsions were studied roentgenographically; it was found that after a single convulsion, one patient presented the same type of compression fracture of the fifth dorsal vertebra.

Of 3 cases who had recovered from status epilepticus, only one showed spinal fractures; these occurred in the twelfth dorsal and first lumbar vertebrae and are described as wedge-shaped deformities of the lower anterior portions of the vertebral bodies with widening of the anterior halves of the discs, associated with considerable sclerosis and roughening in the region of the fractures. Ziskind and Somerfeld-Ziskind[10] have recently reported 3 cases of spinal fracture in the lower dorsal and lumbar regions, describing them as compression fractures without giving the roentgen features. Another of our patients with a diagnosis of meningovascular syphilis suffered with convulsions periodically for seven years. Roentgen examination revealed a fracture of the third lumbar vertebra with compression of the upper articulating surface and upper third of the body. The disc between the second and third lumbar vertebrae is widened but there is no displacement of the body. The roentgenographic characteristics of the fractures in the epileptic and the luetic patients are quite different from those seen after metrazol therapy, and appear to resemble the usual type of compression fracture found in the lumbar region. It is possible that there is a different mechanism of production in the lower section of the spine to account for these variations.

CONCLUSION

It appears rather significant in the light of the above discussion that roentgen examination of the spine should be performed more frequently after convulsions of any etiology. The back pain often complained about in the post-convulsive state should no longer be regarded as merely due to muscular strain without ruling out a vertebral fracture.

SUMMARY

The following is a résumé of our study:

1. After roentgen study of 32 cases treated with metrazol, 14 cases with multiple fractures (43.9 per cent) and 2 questionable compression fractures were found, mainly in the upper dorsal region.

2. The presence of this complication has no fixed relation to subjective complaints, objective clinical findings, the total number of convulsions, or the ages of the patients.

3. Fractures of the spine may result from convulsions of any origin.

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A STUDY OF BONE METASTASES FROM CARCINOMA OF THE PROSTATE

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EVERY roentgenologist is occasionally asked to make a search for bone metastases in a patient known to have or suspected of having cancer. In an institution where large numbers of patients are seen in whom the primary diagnosis is carcinoma such a request is a frequent one, and the result of a well-directed search for such metastases is of great importance in planning the treatment for the patient. Metastatic lesions may be discovered in the course of some other examination and the roentgenologist must be constantly on the lookout for such lesions.

It is obvious that the roentgenologist will be of greatest help to the patient and to the referring physician if, when secondary tumor deposits are found, he can correctly diagnose the primary tumor. The value of the ability to predict the site of the primary neoplasm when the finding of the metastases is incidental to another examination is quite evident, but the character of the metastatic deposits must also be studied when the patient has *one* known primary carcinoma since it is quite possible that the metastases are the result of a *second* primary tumor.

The experienced roentgenologist knows that certain primary tumors give rise to bone metastases of more than normal density, while others give rise to metastases which are predominantly destructive in type. In males the most common osteoplastic metastases are those due to carcinoma of the prostate, but even prostatic metastases are not always of increased density. The present study has been carried out in order to learn the relative frequency of osteoplastic and osteolytic metastases and, if possible, to find some other characteristic feature beyond that of density.

The prostate gland is now known to be a frequent site of primary carcinoma and it is therefore of interest to note that the first clear description of such a case was given as recently as 1854 by Sir Henry Thompson[7] before a meeting of the Pathological Society of London. By 1858 this same author[8] was able to collect only 18 cases from the literature and he considered the disease a rarity, although he suggested that more careful study would show it to be more common. His prediction has been shown to be correct and the disease is now well recognized. It is common knowledge that the initial symptoms may be caused by the metastases and that in a few cases urinary symptoms are absent throughout the course of the disease.

Rich,[6] in a study of "occult" carcinoma of the prostate, found a decided tendency for the early tumors to be situated either laterally or posteriorly in the tissue near the capsule of the gland, with the result that the capsule was not infrequently invaded before the gland itself was appreciably enlarged by the growth of the tumor. This early invasion of the capsule would seem to account for the high incidence of metastases found in carcinoma of this gland.

In an excellent treatise on carcinoma of the prostate published in 1902, Kaufman[5] showed a high incidence of metastases in the lumbar spine and pelvis and also noted their predominantly osteoplastic nature. He remarked on the relative infrequency of pathological fracture as compared with metastatic carcinoma of the breast.

Bumpus[1,2] was among those who first studied a large series of cases with reference to the high incidence of bone metastases. Of 228 cases examined roentgenologically evidence of metastasis was found in 30 per cent. In his earlier series there were 79 cases having bone or other metastases and, of

these, 73 per cent showed metastases in the pelvis. The spine was involved in 66 per cent and the lungs in slightly less than 10 per cent. Other authors have shown a similarly high incidence of secondary deposits in the bony pelvis and a relatively low incidence in the lungs. It is reasonable, therefore, when studying a patient with known or suspected carcinoma of the prostate to direct attention first to the pelvis.

Studies have been carried out with reference to this favorite site of metastasis and theories have been advanced to explain it. At present it seems most reasonable to believe that the invading cells reach the bones of the pelvis and lower lumbar spine by way of the lymphatics and in many cases by way of that particular group of lymphatics which accompany the pelvic sympathetic nerves.[3,4,9] Vascular dissemination occurs less frequently or somewhat later in the course of the disease.

There was formerly considerable difficulty in differentiating the widespread osteoplastic metastases of carcinoma of the prostate from the changes found in Paget's disease. The great improvements in technique, however, which have come with the use of the fine focus tube, better screens and better films have almost entirely wiped out this element of confusion and there are now only rare cases where this differential diagnosis is difficult. In areas of metastatic involvement, either of increased or decreased density, the bone trabeculae are more or less completely wiped out but the adjacent areas show normal trabecular architecture. In osteitis deformans of Paget, on the other hand, the bone trabeculae may almost always be seen through the areas involved, but they are found to be coarser than normal, more widely spaced and may occasionally appear to be grouped together in bundles. The cortical thickening which is so characteristic of Paget's disease, and which is frequently the first sign of this disease is absent in metastatic carcinoma. As a result of the cortical thickening there is frequently a very definite increase in size of the bones in Paget's disease. As a general rule, such an increase in size is not found in metastatic carcinoma. There may occasionally, however, be a definite and at times quite marked increase in size of bones which are the seat of metastasis, but in such bones it is readily seen that the increase in size is not due to cortical thickening but to actual expansion of the bone by the malignant process. Such an expanded bone is the rib shown in Figure 1. Two cases of the present series showed considerable thickening of the pelvic bones. Kaufman[5] showed sketches of similarly thickened pelvic bones and a rib.

Fig. 1. Marked expansion of a rib due to metastatic carcinoma of the prostate.

MATERIAL STUDIED

During the years 1927 to 1938, inclusive, 148 cases were seen in the Palmer Memorial Hospital with a clinical diagnosis of carcinoma of the prostate. Roentgen examina-

Fig. 2. *A*, destructive type of lesion in pubis. *B*, more extensive lesions six months later—now chiefly osteoplastic in type.

tion was done in 108 cases and, of these, 54 showed evidence of bone metastases. It should be noted that the group comprises both early and late cases, some of them having been admitted for radical surgery in the hope of cure and others only for palliative procedures or terminal care. Some cases were seen only once while others were examined several times during a period of months or years. Of the 108 cases studied roentgenologically there was histological evidence of the diagnosis in 59, and of the 54 in whom bone metastases were evident the diagnosis was proved histologically in 23.

Table 1 shows the incidence of metastases in the areas studied and also the relative frequency of the osteoplastic, osteolytic and mixed types. The heading "other bones" includes such areas as ribs, cervical spine, skull and extremities. It should be noted that these areas were not routinely examined and that the relative frequency of metastases in these areas is high as shown in the table due to the fact that these areas were usually examined only if there were localizing symptoms.

Table I

	Cases Examined	Metastases Found	Per Cent	Type		
				Osteoplastic	Mixed	Osteolytic
Pelvis	108	54	50	44	7	3
Lumbar spine	107	32	29	29	3	0
Thoracic spine	98	29	29	26	3	0
Other bones	34	21	61	16	4	1

It is of considerable interest that in the 54 cases in which bone metastases were found, the pelvis was involved in all cases at some time during the period of observation. In 2 cases, however, metastases were first found outside the pelvis but, in each of these, later examinations showed characteristic deposits in the pelvic bones. It is

also of interest that in no case were bone metastases found in the extremities or skull unless there was definite evidence of extensive metastases in the spine and pelvis. The extremities, and particularly the bones beyond the elbows and knees, are recognized as infrequent sites of metastases from any source, but the bones of the cranial vault are relatively common sites for metastases from such organs as the breast, thyroid and kidney.

In those cases in which widespread metastases were found the lesions were not always of the same type in all areas or at all times. There were 3 cases in which the spine and pelvis showed metastases which were almost purely osteoplastic in type but in which the bones outside the axial skeleton showed lesions which were of the destructive or mixed type. In several instances in which the patients were examined on more than one occasion, lesions which were at first almost purely destructive were later found to have changed to the osteoplastic type as they became more extensive. In at least one such case the change from decreased to increased density followed roentgen therapy and the relief of pain. There were several patients in whom metastases were at first found only in the spine and pelvis but in whom widespread metastases were demonstrated some months later.

Fig. 3. This patient had extensive metastatic lesions throughout the skeleton. Note that the normal trabecular structure of the bone is still shown.

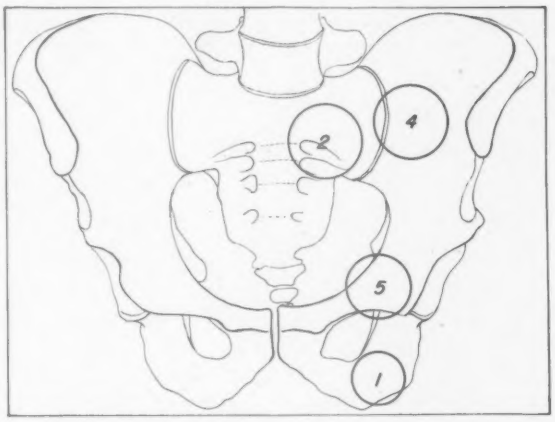

Fig. 4. Sites of early metastases from carcinoma of the prostate. Figures in circles show the number of cases found in those areas.

Of particular interest were the 14 cases in which only a single area was involved when the metastases were first demonstrated. In this group the diagnosis was proved histologically in 8 cases. In 12 of the 14 cases the earliest demonstrable bone metastasis was located in the pelvis. Of the 2 remaining cases the first lesion was in the body of the third lumbar vertebra in one and in the body of the twelfth thoracic vertebra in the other. The location of the 12 lesions in the pelvis was as follows: 5 were in the region of the acetabulum involving its medial wall and the adjacent portion of the ascending ramus of the pubis, 4 were in the ilium just lateral to the sacroiliac joint, 2 were in the sacrum and 1 was in the ischium near its tuberosity. One of these lesions was at first almost purely destructive but later changed to the mixed type. All of the others were predominantly osteoplastic when first seen.

The lesions which were found first in the

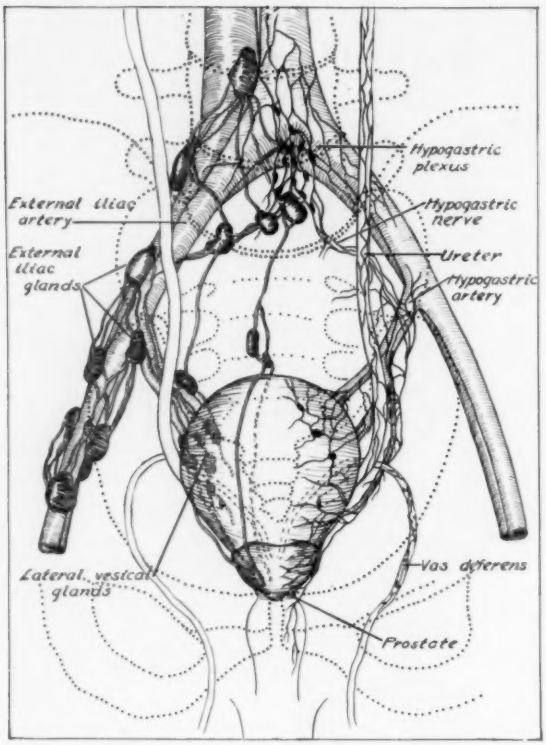

FIG. 5. Diagrammatic drawing of lymphatic and nerve trunks along which metastases spread.

sacrum may perhaps be grouped together with those found first in the ilium close to the sacroiliac joint. Both of these areas are adjacent to the chain of pelvic sympathetic nerves which lie against the posterior wall of the pelvis. This group of nerves carries secretory fibers to the prostate and it was these nerves whose perineural lymphatics were found to be invaded in the autopsied cases studied by Warren, Harris and Graves.[9] They studied large histological sections of the pelvic contents and adjacent pelvic wall and found evidence of perineural lymphatic invasion in each of 8 cases. Ferguson,[3] in a less detailed study of 205 autopsied cases, found evidence of similar invasion in 52 per cent of the cases.

Perineural lymphatic invasion does not appear to be the mode of spread in those cases in which the earliest bone metastases were found in the region of the medial wall of the acetabulum. This area, however, could easily be reached by the chain of lymphatics which run from the prostate to the lateral vesical and external iliac nodes. It seems quite probable, therefore, that the lymphatic vessels served as the means of transport of the disease in at least 11 of the 14 cases in which a single metastatic focus was found.

CONCLUSIONS

Bone metastases from carcinoma of the prostate are predominantly of the osteoplastic type, especially when widespread.

In early cases there is a marked tendency toward localization in the pelvis due to extension of the disease along perineural and other lymphatics.

A metastatic lesion of the osteoplastic or mixed type involving the pelvis or lumbar spine in a man is in all probablity due to carcinoma of the prostate. However, if such a lesion is found elsewhere in the skeleton and if at the same time the lumbar spine and pelvis are free of demonstrable metastases, it is unlikely that the prostate is the seat of the primary tumor.

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THE RADIUM TREATMENT OF RODENT ULCER NEAR THE EYE

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THE radiation treatment of rodent ulcer is both easy and successful, but, in the case of lesions occurring in the vicinity of the eye, certain problems present themselves. Difficulty arises, not only from the peculiar anatomical site, but also from the possibility of causing damage to the eye itself, although my opinion has always been that this danger tends to be exaggerated. The purpose of this communication is to give an account of the experience gained in the radium treatment of rodent ulcer near the eye during the years 1930–1935 inclusive, with special reference to these difficulties, and also to show how eminently satisfactory the results have been. It is contended that implantation in particular can be relied upon as a safe and effective method. A newer short period technique is not described as the cases are not yet of sufficient duration to warrant a dogmatic statement.

During the six years under review, 77 such cases received treatment with radium, and all of these have been followed up. A microscopic diagnosis has rarely been made, since the cases were quite obvious examples of rodent ulcer with one exception which has therefore been excluded, leaving a total of 76 cases for consideration. As is usual in radium therapy, the rationale has been to use gamma radiation, since its selective action is to be preferred to that of caustic beta radiation, and to give at one session such a dose as will prove lethal to the growth while causing a minimum of damage to normal tissues. The inevitable secondary beta radiation around the actual needles or seeds may be disregarded. In the earlier years referred to, radium therapy was in what might be termed the "milligram-hour era," but the methods then developed have proved surprisingly near to those which modern physical measurements would demand. The duration of treatment is these cases has usually been one week, but it should not be inferred that so long a period is necessary for safe and effective radium applications. Recent work in my department has shown that this period may be reduced considerably by variation of the intensity and the total dose delivered. It is too soon, however, to say more of this modification at present.

TABLE I

SITES OF RODENT ULCER NEAR THE EYE

1930–1935

Inner canthus	48
Outer canthus	10
Lower eyelid	14
Upper eyelid	4
	76

The methods have varied according to the special features of the case, but have nearly always consisted of some form of implantation. Surface applicators, however carefully made, are frequently disappointing, since it is very difficult to keep them in perfect position on the skin, and I consider that only rarely are they applicable to this type of case. The chief objection to their use is physical, and is bound up with the question of skin apposition and also with that of attaining the depth dose necessary for all but the most superficial lesions. Implantation either with radium needles or radon seeds is, however, eminently satisfactory for nearly all such lesions and has proved to be a most efficient method of treatment. The different sites occupied by lesions around the eye may now be considered. The duration of the various lesions, according to the patients, varied from two months to twenty years.

INNER CANTHUS

Case Details. This is by far the commonest site for rodent ulcer near the eye and is also one of the more difficult to deal with. The group of 48 patients consisted of 27 males and 21 females, the youngest being thirty-seven and the oldest ninety years of age.

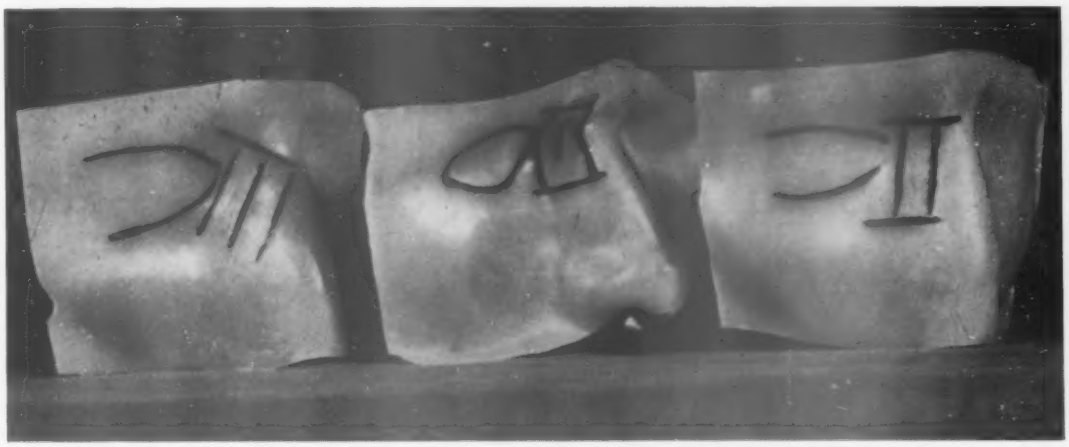
In 10 cases there had been previous unsuccessful treatment with CO_2 snow, surface radium, or operation, singly or in combination. Such antecedent factors were found not to affect materially the success of treatment, but they did provide the additional problem of how to deliver with safety an effective dose to tissues the vascularity of which had been impaired. The chance of undesirable post-irradiation change is naturally greater in such cases.

The extent of the lesion was such in 11 cases that special mention was made in the clinical record of involvement of one or both eyelids, but again the treatment was able to cope with this since all these have remained well. One extreme case presented a growth probably starting at the inner canthus and spreading along both eyelids to the outer canthus; it is hardly surprising that this patient was one of the few to suffer ocular damage.

Technique. It has already been stated that surface applicators are no longer used and it will therefore suffice to describe the implantation methods. Radon seeds form an easy and convenient means of irradiating many of the inner canthus lesions, and may readily be arranged so as to conform to physical requirements, some form of circular distribution being the most usual. The seeds used contained 1 to 1.2 millicuries with filtration of 0.5 millimeter platinum and were introduced under local anesthesia. The skin is rendered clean with proflavine oleate 1 per cent in liquid paraffin, and 2 per cent novocaine used for the anesthesia. Any existing sepsis must be dealt with before treatment; after removal of any crusts, this proflavin oleate preparation has been found a most effective dressing. It is important to inject as little anesthetic as possible, since the lax tissues tend to swell very readily, rendering accurate work difficult. An ordinary Muir's seed introducer was employed. I have found this an effective method, but believe that more accurate and uniform dosage is possible with the use of radium needles, the position of which in the tissues may be checked more readily by palpation. Moreover, a higher proportion of patients treated with seeds have complained of lacrimation afterwards; but this may be a coincidence.

For implantation of radium needles the preliminary steps are similar to those just described, but the skin is then punctured with a sharp trocar and the needle introduced with a rotatory movement. The skin is steadied during this process, so that it does not yield before the pressure and disguise the true position of the needle which is verified by palpation. The principle of treatment has been to adapt to the special requirements of the individual case, a simple closed plane constructed with five radium needles arranged in a group of three parallel needles closed at each end. This can usually be done at the inner canthus, though at times one end of the plane has to be left unclosed; in this case the needles should be placed so that the lesion is towards the normal end of the plane. The needles which have usually been employed during the past few years are 27.7 mm. long with active length 16.2 mm., filtration 0.5 mm. platinum, and content of 1 mg. radium element. It will be found after some experience that this length is quite suitable for a majority of inner canthus cases. Such a plane, with needles not less than 1 cm. apart, has been left in place for 168 hours routinely. This period was arrived at in the early days as a result of clinical experience and observation, and has been justified since it has stood the test of time, both as regards efficacy and freedom from post-irradiation damage. Since having facilities for physical investigations, I have found that the dose about the center of the plane approaches 8,000 r, though the average will be between 5,000 to 6,000 r, and this indi-

cates that some reduction is probably permissible for rodent ulcers. If such reduction is made, it will be for economy in time and not through any fault in the present dose level. The question of treating rodent lesions over a short period of time is a totally different one, but, as has been stated, this is also receiving my attention. During treatment the eye is kept open and is not covered by any dressing, watery acriflavine drops 1:1,000 being used regularly; otherwise purulent conjunctivitis may occur. In the early years, needles of similar radium content but shorter length were frequently used. These had of necessity a higher linear intensity and so, though effective, were found liable to give more post-irradiation change even in shorter treatment times. Our knowledge of the influence of dose rate as well as that of total dose was naturally less in those days.



A *B* *C*

Fig. 1. Three wax impressions of face marked to show positions of implanted needles as described.

The method is illustrated by Figure 1 having three wax models marked so as to show the positions which needles will occupy after implantation. The arrangements shown have been taken from actual case records; they are capable of great variation as the individual case may demand. *A* and *C* were constructed with 27.7 mm. needles and it will be seen that *A* could, if necessary, be closed below, in addition, or instead of, above according to the position of the lesion. *B* is a case where seven short needles had to be used owing to the configuration of the parts which would not accommodate the normal length. At the sites presently to be discussed, similar principles guided the implantation methods and so further description of the technique can be omitted. Some degree of moist desquamation is expected to follow the treatment, and with its occurrence an oily type of dressing is essential. Proflavine oleate, ammoniated mercury 0.5 per cent, or vaseline alone are used according to what the skin seems to need. A simple eye wash may be called for alone or with argyrol 10 per cent drops. The latter should not be used for more than a short period to prevent any development of argyrosis.

Results. Only 3 cases were treated by *superficial application*, this method being found unsuitable as stated. One has remained well to date, and one showed a small recurrence which was treated successfully by excision. The third also showed recurrence and was treated with radium again, the skin being in good condition. The method was by implantation using needles 27.7 mm. long containing 0.5 mg. radium element in an active length of 16.2 mm. with filtration 0.5 mm. platinum; such a low intensity implantation spares the skin and is very useful for a second treatment in

the rare event of this being called for. The needles were left in position for two weeks, and this case remains well to date without skin damage.

Seven cases were treated with *radon seeds* as described. Five have remained well to date; 2 died of other cause one year after treatment with the lesion healed. Three of the survivors have a definite complaint of lacrimation, and post-irradiation change in the skin seems rather more prominent in these cases than in the radium implantation series. The numbers concerned vary so much, however, that comparision is difficult. One of the radon cases had bilateral lesions, and both of these are healed.

Radium implantation was the method employed in the remaining 38 cases, and these had variable sizes of lesion, the eyelids being involved in 11 instances. One presented an edge recurrence five months after implantation and this was excised. Another case was of ten years' duration, and had recurred after the use of both CO_2 snow and radon applications. The tissues were much scarred before radium treatment was given, and the lesion recurred six years later. Since then it has required treatment both by surgery and with radium; the condition appears stationary at the moment but there can be no doubt that disease is still present (Table II). In only 3 instances are there records of trouble with lacrimation. The skin has occasionally shown some degree of post-irradiation change, particularly in the early cases where treatments of high intensity type were used.

Ten patients died of some other cause a period of years after treatment, their lesions remaining healed; the others are well at the time of writing.

TABLE II

RESULTS

Number of Cases	Well to Date or Death from other Cause (One Radium Treatment)	Well (Surgery Following Radium)	Well (Second Radium Treatment)	Failures
Inner canthus 48	44	2	1	1
Outer canthus 10	9	1	0	0
Lower lid 14	12	0	1	1
Upper lid 4	3	1	0	0
76	68	4	2	2

OUTER CANTHUS

There were 10 patients with lesions at the outer canthus of the eye. Five of these were males and 5 females, the ages varying from thirty-nine to eighty-two years. Two patients had received previous treatment with caustics or CO_2 snow, and in 4 the growth had spread to the eyelids. Seven were treated with simple radium needle implantation on the principle already described, the method being much easier to carry out in this situation. The remaining 3 had superficial applications of radium; in one of these further treatment by implantation was found necessary. One case required excision two years after the original treatment, and 2 were satisfactorily healed at the time of death from some other cause. The remaining 7 patients have remained healed up to date.

LOWER LID

There were 14 patients with lesions in this location, 5 being females and 9 males, the ages varying from forty-seven to eighty-two years. Previous treatment with CO_2 snow, surface radium, or by surgery

had been carried out in 4 cases. Owing to the mobility of the part, surface application is rarely suitable, but 2 cases were treated in this way and have remained well. The remainder were dealt with by implantation which is satisfactory even when the growth has extended to the lid margin and conjunctival surface; cosmetic results are good. Among the 12 cases treated with implantation I encountered two years after treatment one tiny recurrence which was successfully treated with a beta-ray plaque, and one extensive lesion in a patient, aged eighty-two, with mental symptoms which rendered him a most difficult subject for treatment. This latter case was a failure. Two of the remaining patients died of some other cause with their lesions healed, one and four years after treatment respectively. The others are well at the time of writing.

UPPER LID

There were only 4 cases with lesions affecting the upper eyelid, 2 being males and 2 females, with ages varying from fifty-three to seventy-one years. One of the latter had an extensive lesion, recurrent after excision some years before, affecting the upper eyelid, region of eyebrow, and side of nose. It was treated with a surface apparatus, a method which was not ideal from the physical point of view, and there have been two small edge recurrences both of which were excised. Since then this patient has had two rodent ulcers in other locations successfully treated with radium. Four years after the first treatment with radium, she was found to be suffering from pernicious anemia but is now doing well under medical treatment. The remaining 3 cases presented lesions limited to the upper lid and one of these had previously been excised on two occasions. All were treated with radon seeds, and remain well as far as the growths are concerned. In 2, however, serious ocular changes have occurred and I regard this site as one where a certain amount of danger is associated with treatment as it was given at that time.

CONSIDERATION OF RESULTS

Reference to Table II will show that the treatment can be regarded as successful having regard to the special difficulties which have been outlined. Of the 76 cases, 68 have remained healed after primary treatment (89.4 per cent), 4 have required in addition some minor surgical procedure, but in 2 of these the original treatment should have sufficed; the method adopted was not ideal, too much being attempted with a surface applicator. Another 2 cases are well after a second treatment with radium, and again one of these probably recurred because of faulty choice of technique. Thus, 3 of the 6 cases requiring extra treatment may be regarded as examples of faulty technique, but it should be emphasized that these 6 cases did not fall too far short since relatively minor surgical or radiation procedures completed the healing (97.3 per cent). This accounts for 74 cases, and the remaining 2 represent the only failures; in each of these, conditions were very unfavorable to begin with.

These results may be taken as representing an accurate idea of what can be done by the use of radium, since only 2 cases have been rejected for treatment during the period under review. One was a woman, aged eighty-five, with a small rodent ulcer at the outer canthus. She was very frail and had lax atrophic skin, so that excision was felt to present the easiest method of dealing with the lesion. The second patient was also a female with a very small and readily excisable lesion on the lower lid, and again surgery was advised. There would have been no technical difficulty in treating either case with radium.

EFFECTS OF RADIATION ON THE EYE

It is essential to consider briefly the effects which radium, applied at the sites described, and in dosage suitable for dealing with a malignant growth, appears to have had on the eye. The usual immediate effect is merely the production of some conjunctival injection occasionally associated with slight edema. The reactive changes in

the skin are similar to those observed during the application of radium to the integument in general and, if normal dosage for the duration and intensity of treatment be adhered to, they will subside satisfactorily. These immediate changes are of short duration, and it is the latter effects which are of importance. Two of these may be briefly dismissed; they comprise epilation which may be met with according to the site irradiated, and excessive lacrimation to which reference has already been made. Interference with the drainage of tears is rarely a complication giving rise to much trouble in my experience, and possibly it would be met with less often if dilatation of the punctum were carried out after treatment of the inner canthus lesions as soon as watering appeared.

Many of the patients with rodent lesions near the eye are past middle age and the incidence of certain ocular changes is likely to be high in any case; moreover, the observer may meet with abnormalities after treatment and the part played by irradiation in their causation may be very doubtful. It is therefore suggested that a preliminary ophthalmological examination should be carried out in all these patients. Simple ocular lesions may be stirred up by irradiation for it is well known that radiotherapy in normal dosage may adversely affect inflammatory conditions and cause vascular disturbance, in contrast to the beneficial effect often claimed for the treatment of such conditions by minute doses. Such preliminary examinations were not possible for most of the series dealt with here, but, during the period under review, any case complaining of eye symptoms, or showing any ocular abnormality, was sent for special examination so that no gross lesion would be missed. Since the opening of the Eye Department at the Western Infirmary, Professor Ballantyne and his assistants have kindly undertaken routine observations before and after treatment. The post-irradiation complications usually regarded as likely in the eye itself are corneal ulceration resulting from high dosage on the eye itself, or from secondary ectropion; cataract; and glaucoma. The incidence of ocular abnormality in this series will now be dealt with and all changes observed will be noted whether or not they appear to be connected with irradiation.

Of the *inner canthus* group only 3 cases out of 48 show any effect in the eyes. The first of these, a woman of fifty-six, had rodent ulcers at each inner canthus treated with seeds in 1935, and there is now slight opacity at the posterior part of the lens in each eye. There was no ocular examination before treatment; the visual acuity is now R 6/36 and L 6/60. The second patient was a man of the same age with a very extensive lesion involving the inner canthus and both eyelids as far as the outer canthus. It is not surprising that corneal ulceration caused loss of the eye some months after his treatment in 1930. The cornea must have been exposed to a high dosage and there was coincident sepsis. Examination of the eyes in the third case, a man of fifty-seven, revealed before treatment a maturing cataract in the opposite eye; so far there has been no sign of cataract on the treated side. This large group, therefore, presents only 2 cases showing change due to irradiation, and the one with serious ocular damage had an extremely advanced malignant growth which remains healed.

There are again 3 cases in the *outer canthus* group—10 in all—where any ocular change was seen. One of these suffered before treatment from recurrent corneal ulceration in each eye but the incidence and severity of this has not been greater since the use of radium. A woman of fifty, however, with a lesion affecting the right outer canthus and adjacent parts of both eyelids, showed seven years after treatment some opacity in the lens on the same side, with atrophy at the fundus and pigmentation at the disc; the left lens is clear but the macular region shows some pigmentary change. The visual acuity is 6/12 for both eyes. More serious changes were seen in the third case, a man of sixty-nine, who was treated for an extensive lesion affecting the

right outer canthus, parts of both eyelids, and part of the eyebrow region. Seven months later corneal ulceration and iritis developed, the eye becoming disorganized. Again, therefore, there are 2 cases in this group showing post-irradiation changes in the eye, but in one of these the malignant lesion was of an advanced character spreading to the soft tissues above the eye. The fundal changes in the 2 cases are not regarded as being due to irradiation.

The 14 cases with lesions of the *lower lid* include 2 examples of ocular damage. The first of these, a woman of fifty-four, complaining of dimness of vision three years after treatment. On examination a greyish patch probably due to gliosis, and clearly without any relation to irradiation, was seen in the opposite eye. The other patient was a woman of seventy-three with arterial hypertension and renal insufficiency. She had defective vision on both sides with some opacity in the nucleus of each lens accompanied by floaters in the vitreous and some hemorrhages with patches of exudate. The relation of the opacity to irradiation appears very doubtful, and so no case in this group can be said to show definite irradiation damage.

The situation has been different in the case of lesions affecting the *upper lid*, and the treatment adopted during the period under review did seem to expose the eye to greater danger of complications; work is proceeding on a modified technique to minimize this. Of the 4 cases treated, 2 showed serious changes with loss of vision, due to glaucoma in one instance, and in the other to a peculiar increase of vascularity spreading from conjunctiva and iris into the eye; the process is probably comparable with the formation of cutaneous telangiectasia. One other patient, a woman of fifty-three, showed two years after treatment high myopia in both eyes with floaters in the vitreous, degenerative changes in the fundi, and slight opacity in the lens on the treated side; the visual acuity is now R 6/18 L 6/24. Only the lens opacity can be attributed to the use of radium.

There are therefore 7 cases, out of a total of 76 treated, where some obvious change in the eye may have been caused by irradiation (Table III), but only in 4 of these was the change severe or disabling, the other 3 suffering merely from diminution in visual acuity. If the 4 upper eyelid lesions, with their abnormal incidence of complications, be excluded, there were only 2 patients with serious eye damage in a total of 72 treated. Still more detailed observations are going on regarding post-irradiation changes in the eye, but the present account includes anything which would have practical application to the question of eye damage affecting the sight.

Table III

Incidence of Ocular Complications

	Total Cases	Late Eye Changes Seen in:	Change Probably Due to Irradiation in:	Loss of Vision in:
Inner canthus	48	3	2	1
Outer canthus	10	3	2	1
Lower lid	14	2	0	0
Upper lid	4	3	3	2
	76	11	7	4

The dose received in the region of the lens, and at the periphery of the iris on the side nearest the radium, has been determined experimentally. A wax cast of the face was employed, and radium needles embedded in this as they would be implanted in the tissues. Suitable Sievert chambers were then placed at the points indicated, and the dose determined ionometrically. The source of radiation in these experiments has been the simple closed plane already described as consisting of five needles of total length 27.7 mm. with content 1 mg. These needles have been suitably arranged in the wax at inner canthus and lower eyelid, but, in the case of the upper eyelid, two parallel needles only were employed as being more consistent with the possible arrangement in this situation. In the latter case, readings were taken

with the needles in such positions as they would occupy with the eye closed, and then again with the eye open. It is fully realized that an implantation with this actual size of needle is unlikely in the upper lid; the radium would no doubt be split into shorter containers of lesser content. All that was desired, however, was a reading enabling the incidence of radiation upon the eye to be compared with that received from the other implantation sites. The dose received by the eye, as recorded in Table IV, can only be an absolute reading in the case of our method of treatment, but it may be taken as showing in what proportion the various implantation sites would contribute.

TABLE IV

	Inner Canthus	Outer Canthus	Lower Lid	Upper Lid	
				Open	Closed
Pupil	9.0	Taken as not greater than doses for inner canthus	16.7	23	35
Iris	9.0		16.7	27	35

Figures represent readings in roentgens per hour.
The iris readings are taken on the side nearest the implant and are therefore maximal.

The figures indicate that *the upper lid* is the most dangerous part to implant as far as the eye is concerned, and this coincides with the clinical opinion already given. It will be recalled that special methods are being elaborated by which it is hoped the risk will be reduced materially. The inner and outer canthi, and even the lower lid, have never seemed clincially to present the same possibility of complications, and the total dose received during a week's implantation would therefore appear to be within the safety limit in most cases. At the moment I am therefore placing the tentative figure of rather less than 3,000 r (gamma) delivered in a week as the maximum dose to be tolerated by the eye (16.7×168 hours = 2,805.6 r). Since lens opacity has been observed in one inner canthus case, it must at present be assumed that as little as approximately 1,500 r (9.0×168 hours) may cause this change; but there was no control examination before treatment.

DISCUSSION

No extensive review of the literature seems necessary since a number of detailed accounts of this nature exist and are readily available. For this reason, only brief reference will be made to a few of the writings which have been consulted.

All who are interested in the effects of irradiation on the eye will be familiar with the valuable work of Desjardins[2] who has compiled and analyzed an exhaustive survey of the literature on the subject with reference to both roentgen rays and radium. From this account one can get an excellent idea of the pathological changes which may occur after exposure to radiation, and it is not necessary to refer further to work which is so well known. It is not always easy, however, and sometimes impossible, to get a clear idea of the dose levels which produce these effects, since it is comparatively recently that dosage has been reduced to a matter of exactitude as regards dose units, to say nothing of the importance of a full statement of dose factors. Desjardins has stated how much difficulty exists in this respect as regards reviewing the clinical and experimental applications of radium recorded in earlier literature, and this led me to consider the probable maximal doses received by the eye.

My own observations in this series of cases are based on the treatment of limited volumes of tissue near the eye with normal therapeutic doses of radium and would appear to conform reasonably closely to what Desjardins, and Colwell and Russ,[1] have described, although the degree of tissue change after treatment has not been

severe as a rule. For example, a more advanced degree of reactive and late change, both superficial and deep, is recorded by Stallard[5] both from his own experience and from reference to the literature, but most of his own patients had lesions for which the eye itself had to be irradiated locally and therefore exposed to higher dosage. The *skin* of the eyelids and the hairs there naturally behave as these structures would elsewhere. Ordinary desquamation and epilation will be encountered, and no trouble need be anticipated provided the dose is known to be within ordinary therapeutic limits, as should always be the case. The situation is similar as regards the *conjunctiva* which will normally share in the inevitable reaction; only rarely do a few dilated vessels persist. The *cornea* is regarded as slightly more resistant, and only when very high dosage has been applied directly over it would one expect to see any interstitial change, though epithelial dystrophy may appear, usually as a temporary phenomenon. It will be recalled that corneal ulceration was seen in only 2 cases out of the present series, and that in one the whole of both eyelids was involved by growth while the other presented infiltration of right outer canthus, parts of both eyelids, and part of the eyebrow region. A third instance of ocular damage apparently beginning in the region of the cornea and conjunctiva was furnished by an upper lid lesion, this being the case (see Table IV) in which a peculiar increase in vascularity, no doubt telangiectatic, developed in the superficial tissues and spread into the eye affecting the iris.

Since the radiation from such implantations as are used here will fall off very quickly in intensity, it is not surprising that deeper structures in the eye, such as the *retina*, should not show gross change, quite apart from the fact that they are tissues of a radioresistant character. The general opinion would appear to be that the region of *iris* and *choroid* is to be regarded as standing radiation well, but we have in this series one case of glaucoma following treatment of an upper lid lesion. No doubt this was due to some interference with the adjustment of pressure within the eye, but the subject is one upon which the literature throws little light, though it is obvious that both at the time of reaction and later, vascular changes will take place, the effects of radiation in this direction being well known. Colwell and Russ[1] state that predisposing causes of post-irradiation glaucoma are unknown.

The *crystalline lens*, on the other hand, must be regarded as fairly sensitive to radiation even in adult patients. Desjardins stated originally that the lens was resistant in the adult, but he later amended this, and, in 1938,[3] stated that this opinion had to be revised. The matter is obviously one of great practical importance, not only as regards the type of case dealt with here, but also in the irradiation of any lesion near the eye. As has been stated, we encountered 4 cases where some lens opacity was later observed, but none had had previous ophthalmological examination. It may be recalled that one of these belonged to the upper lid group where the technique then used involved relatively high dosage at such vulnerable parts, and that another was a patient suffering from cardiorenal trouble the opacity appearing in both eyes, although only one side was treated; the relation to irradiation in this latter case is obviously most doubtful. There are therefore only 2 patients, suffering from inner and outer canthus lesions respectively, in which opacity followed a normal type of treatment not thought to involve special risk.

It will be seen that I have encountered the usual sort of complications, but in no great frequency having regard to the number and types of cases treated; as has been explained, I hope that this incidence will be reduced in the future. Martin[4] gives an excellent account of eye changes following irradiation in this vicinity and suggests that, in implantation near the eye, an increase in filtration from 0.5 to 0.8 mm. platinum has been helpful in preventing

complications. Such an alteration could only mean a very slight decrease in the softer components, some increase in characteristic platinum radiation, and a drop in intensity of about 6 per cent. The latter change would appear to be the only one likely to produce any effect, but my own experience is such that I would confidently continue treatment with the present radium needles which are screened with 0.5 and 0.6 mm platinum. My experience, reviewed in the light of correlating the observed effects of irradiation with the experimental values noted in Table IV, would lead me to suggest at the moment that gross damage to the eye in general is unlikely unless it receives more than 2,800 r, but that opacity might appear in the lens, though rarely, with as little as 1,500 r. These figures refer to gamma radiation delivered continuously over a period of one week. The careful preliminary examination now undertaken will amplify these observations, which are being considerably extended through Professor Ballantyne's cooperation.

No opportunities for microscopic examination of irradiated tissue presented themselves, but it may be taken that the usual vascular and stromal changes would be apparent since alterations in vessel walls, in amounts of fibrous and elastic tissue, and so on, must always follow even therapeutic doses. Only when these inevitable results of irradiation appear in excessive degree as a result of mistaken dosage should undesirable sequelae be apparent.

SUMMARY

Methods of treating rodent ulcers near the eye with radium are described, and the results given for a series of 76 patients dealt with during the years 1930–1935. All cases have been followed-up to the end of 1938—a period of three to eight years. The question of damage to the eye is described in the light of the experience provided by these cases, and its incidence in this series is stated. A tentative statement as to the probable dose producing such ocular effects is made as a result of experimental observations.

I have much pleasure in acknowledging the cooperation of members of the Visiting Staff of the Western Infirmary in giving me every facility in their wards to carry out treatment with radium; in addition, many ophthalmic examinations have been performed by Professor Ballantyne and his Staff. My thanks are also due to Dr. John Thomson, Physicist to the Radium and X-ray Departments, for carrying out the physical estimations.

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RADIUM TREATMENT OF VASCULAR NEVI

AN ANALYSIS OF 152 CASES SEEN DURING 1928–1938*

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IN 1907 Wickham and Degrais[23] published the results of their fundamental clinical investigations dealing with the effect of radium on angiomata. Numerous articles on this subject have since appeared and it may be assumed from their content that radium is the most valuable single therapeutic agent in the treatment of these lesions. Because of the great variety of angiomata which are observed clinically, several more or less elaborate systems of classification have been proposed. For practical purposes one recommended by MacKee[13] seems to be simple, comprehensive and to serve the purpose well. He divided the angiomata into nevus flammeus (portwine mark), nevus vasculosus (strawberry mark) and angioma cavernosum (cavernous angioma). There occur, of course, quite frequently mixed types where, for instance, a subcutaneous cavernous angioma is covered by skin involved with a portwine or strawberry mark or both. In 3 patients of our series large sized subcutaneous cavernous angiomas were found covered by normal skin.

The etiology of vascular nevi is still a debated question although several hypotheses have been advanced. According to Geschickter and Keasbey,[9] who analyzed a series of 570 angiomata, Ribbert's theory assuming their development from embryonic rudiments is most plausible. Histologically the capillary angioma (nevus flammeus and vasculosus) consists of a fine network of capillaries while the cavernous angioma is composed of dilated blood spaces with thin walls. The subject is discussed in great detail in the paper by Geschickter and Keasbey quoted above.

One fundamental question which is asked frequently both by the family physician as well as by the parents is "Should a vascular nevus be treated at all and if so when is the best time to start treatment?" Cases have been reported where an angioma disappeared spontaneously but apparently this is so rare an occurrence that treatment seems advisable.[22] We have seen in ten years only a single child with an extensive angioma of the forearm which became secondarily infected and disappeared almost completely after antiphlogistic treatment, leaving, however, a very noticeable scar after healing.[18] As to the best time for instituting therapy, the consensus is the earlier the better, certainly during the first year of life, and two months might be considered as the minimum age.

TREATMENT

a. Methods

A number of non-radiological methods have been advocated for the treatment of vascular nevi; although we have had no personal experience with any of them, they will be briefly outlined. One of the oldest procedures is that of "freezing" by means of solid CO_2. It is still useful for small lesions, preferably on unexposed parts of the body.[3] Surgical excision either with a scalpel or with the endotherm knife still has a place; MacCollum[12] believes that operative removal offers the best results. More recently the injection of sclerosing solutions has been recommended, and a mixture of quinine and ethyl carbamate was found to be most suitable.[2] The results obtained are said to be equal to those following radium

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therapy, especially in lesions about the eyes, on the lips, sides of the face or on hands and wrists.[3]

The radiation treatment of nevi is limited to the use of roentgen rays or radium. Although roentgen radiation of either moderate or higher penetration[1,15,16] is effective in treating them, radium has become the agent of choice in this country. Ulceration of the nevus and secondary infection are no contraindication to radium therapy except that the doses should be smaller than for the non-infected type; treatment of the inflammatory process by roentgen rays first and followed then by radium therapy of the nevus proper may also be considered.[18] There exists a fairly general agreement that the portwine mark is not a suitable subject for roentgen and radium therapy,[5,13,19] in spite of the fact that satisfactory response has been seen in small lesions treated early.[1] Grenz rays[10] have also been advocated and improvement occurred after "blistering doses" with the Kromayer lamp[12] or the so-called Intensol lamp,[11] a water-cooled high-pressure quartz mercury vapor lamp. Since radium was used exclusively in our own series the discussion of the technique of treatment will be limited to the various types of radium applicators.

b. Technique of Radium Therapy

1. *Radium Plaque.* The simplest radium applicator suitable for the treatment of strawberry marks and superficial cavernous angiomata is a glazed radium plaque, either full or half strength, filtered through from 0.1 mm. Al to 2.0 mm. brass. With the aluminum filter beta rays are transmitted and considered by some as highly efficient in the treatment of superficial lesions,[13] although others insist on the superiority of gamma rays in all cases.[3] The plaque is usually applied in contact or within 2 mm. of the skin surface since small lesions have to be screened by a lead mask of at least 1.5 mm. thickness. According to MacKee,[13] at contact a 2×2 cm.^{2} 10 mg. plaque with a filter of 0.1 mm. Al should be left in place not longer than twelve to fifteen minutes in order to avoid an erythema. For smaller areas the exposure time can be lengthened in proportion. The treatment should not be repeated before a month and sometimes not before from six weeks to two months, depending on the reaction. If a filter of 2.0 mm. brass is chosen 70 mg-hr. in contact or 200 mg-hr. at a distance of 1 cm. are suggested;[3] this should correspond to approximately 60–70 per cent of an average erythema dose.

2. *Screens.* For lesions over 3 mm. thick, gamma rays from heavily filtered screens (2.0 mm. brass or equivalent) are indicated, usually at distances of from 1 to 3 cm. depending on the depth of the involvement. As an example, MacKee[13] states that a 2.0 mm. brass screen loaded with 25 mg. radium element at 2.5 cm. distance and covering an area of 2.5 cm.^{2} of skin surface can be left in place for two hours without causing an erythema. If multiple screens are needed, imbedded either in molds prepared of dental compound or packed in so-called trays, about 20 mg-hr. per cm.^{2} at 0.5 cm. distance[4] or 800 mg-hr. for a rectangular applicator of 4×5 cm.^{2} at 3 cm. distance[3] is considered sufficient. The interval between treatments given in this manner should be at least three months.

A new method of applying radium screens based on mathematical calculation has been described by Strandqvist:[21] "The principle of the arrangement makes use of standard applicators consisting of individual glass capsules for each radium tube by means of which the tubes are always fixed at exactly the same distance from each other and from the surface of the skin. Thus the intensity of the γ-radiation from every applicator can be previously determined and the treatment time for any desired dose can be read off directly from a dosage chart." This method proved suitable in the treatment of deep as well as superficial cavernous angiomata. The greatest advantage is seen in the fact that 94 per cent of all cases required only one treatment and the other 6 per cent two treatments. In 72 per cent of 285 cases the lesion disappeared

Fig. 1

Fig. 2

Fig. 1. Strawberry mark on scalp. In November, 1937, 7.5 mg-hr. (0.1 mm. Al, contact); repeated in December, 1937, January and March, 1938.
Fig. 2. Lesion completely disappeared. Last examination in July, 1938.

without leaving a scar. The treatment is given during the first three months of life with a maximum "average dose" in 1 cm. superficial tissue layer of 800 r. This "average intensity" is defined as being equal to the sum of the surface intensity, four times the intensity at a depth of 5 mm. and the intensity at a depth of 10 mm. divided by 6. The doses applied were calculated in roentgens and it appeared that the "average dose" in the 300 cases treated varied between 600 and 1,100 r while the surface dose varied between 1,200 and 2,200 r. In his conclusion the author stresses, however, that "the treatment must always be individualized to a certain extent. In the individual case attention must be paid to the age of the patient, the size and type of the hemangioma, the state of the covering skin, the location and the condition of the surrounding normal tissues. Hemangiomas covered by sensitive skin may be treated with an 'average dose' of 700 r and those covered by dense skin with 850 r."

3. *Radon Seeds and Radium Needles.* Interstitial radium therapy with various types of implants has been recommended by a number of radiologists. Withers[24] and Brown and Byars[7] obtained good results in bulky angiomatous tissue. Schmidt[20] used steel needles, Edwards[8] monel metal needles (1 mg. radium, 2.5 cm. length, 0.3 mm. wall thickness, left in situ one to three days), also radium element implants (1.3 mg., 0.3 mm. Pt, 7.5 mm. length), Anzilotti[4] and Baensch[6] radium needles with a wall thickness of 0.5 mm. Pt. The latter has available needles of 2.5, 3.0 and 4.5 cm. length with a content of 1, 2 and 4 mg. radium element. The dose is 1 mg. per cc. of angiomatous tissue and the needles usually remain in place for two days. Additional therapy should not be considered before two to three months have elapsed. No hemorrhage, no retardation of growth and no late injuries were encountered.

c. Our Technique

We have tried above all to individualize the treatment and refrain from adherence

to any hard and fast rules, except for the observance of certain maximum doses which assure the avoidance of an erythema. For superficial lesions, a combination of β and γ-rays (radium plaque, 0.1 mm. Al) has proved very effective and free from undesirable sequelae if no erythema is produced. Occasionally the response is very quick and cosmetic results are excellent (Figs. 1 and 2). This applicator is also of value in the treatment of the discoloration of the skin in the combined type of lesion especially after the subcutaneous part of the angioma has responded to γ-rays and marginal areas of strawberry mark still remain. We have found that a 2×2 cm.^{2} 10 mg. radium plaque filtered through 0.1 mm. Al can be applied for up to an hour on an area of 1 cm.^{2} in the average case without causing a reaction, and correspondingly less for a larger area, down to ten to fifteen minutes for the full size plaque. The intervals between treatments vary from four to eight weeks. If the lesion involves the lid, eye shields are inserted for the protection of the eyeball (Fig. 3).

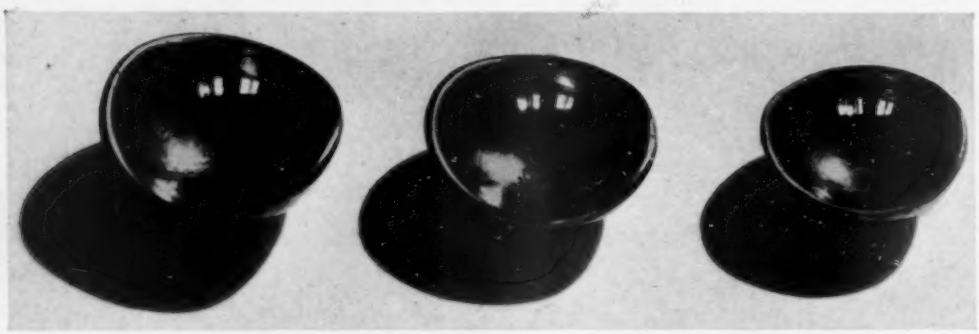

FIG. 3. Eye shields. (Reproduced through the courtesy of *Colorado Medicine*.)

For lesions thicker than 0.5 cm. or subcutaneous angiomata, we use radon screens either filtered through 0.5 mm. Ag plus 1.0 mm. brass or through 2.0 mm. brass at a distance of from 1 to 3 cm. which is maintained either by wood or by dental compound if a mold has to be made. According to the thickness of the lesion, the dose per square centimeter of surface has varied from 20 to 40 mc-hr. but a single dose of 300 mc-hr. at 3 cm. distance has never been exceeded. Large areas are treated by mul-

FIG. 4

FIG. 5

FIG. 4. Large cavernous angioma on right forearm. In December, 1935, 300 mc-hr. (3 cm.); repeated in February, May, November, 1936, and in June, 1937.

FIG. 5. Satisfactory cosmetic end-result. Last examination in December, 1937.

Fig. 6

Fig. 7

Fig. 6. Large cavernous angioma, right temple, covered by normal skin; 300 mc-hr. (3 cm.) in March, June and September, 1935, in May, 1936, and in September, 1937.

Fig. 7. Marked reduction in size of angioma; no late reaction in overlying skin. Last examination in September, 1939.

tiple applicators leaving a margin of 3 to 4 mm. between exposed fields to avoid overlapping and excessive "borderline reactions." All applicators are securely fastened by means of adhesive tape and if possible under slight pressure. Intervals between treatments are from three to six months. Patience is indicated in our opinion because a conservative approach assures better end-results and reduces the possibility of late reactions (Figs. 4–7).

In the last two years we have occasionally inserted radium needles of 2.5 cm. length, with 1 mg. radium element content and a wall thickness of 0.5 mm. Pt. We found that parents are not very enthusiastic over this procedure and only reluctantly give permission to proceed. Even

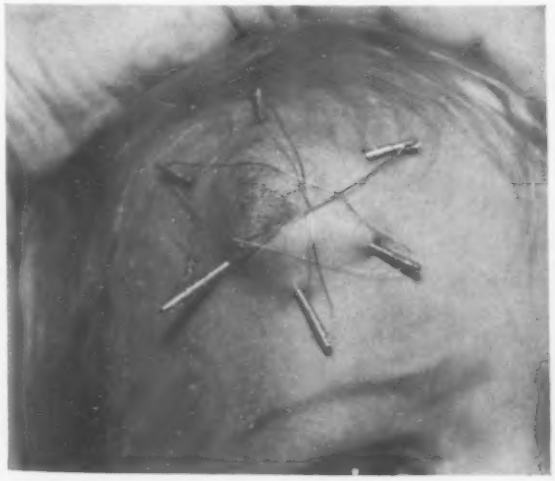

Fig. 8

Fig. 9

Fig. 8. Cavernous angioma in right frontal region. Six 1 mg. platinum radium needles in situ on August 30, 1939.

Fig. 9. Good response of lesion to treatment. Appearance on December 30, 1939.

TABLE I

DISTRIBUTION OF NEVI AS TO AGE, SEX AND TYPE

Age	Sex M.	Sex F.	Portwine Mark	Angioma S.	Angioma D.	Lymphangioma	Nevus Pilosus	Total
0– 2 mo.	1	6	—	3	4	—	—	7
2– 6 mo.	15	44	—	45	14	—	—	59
6 12 mo.	15	27	1+2*	17	22	—	—	42
1– 3 yr.	4	16	—	7	13	—	—	20
3–10 yr.	4	2	—	4	2	—	—	6
Over 10 yr.	12	6	1	7	8	1	1	18
	51	101	4	83	63	1	1	152

* Treated by ultraviolet rays.

with our limited experience, we feel that the method is certainly very effective[17] and should probably be employed more widely. We insert the needles approximately 1.0 to 1.5 cm. apart and retain them by sutures. They are left in place for forty-eight hours (Figs. 8 and 9). In one case hemorrhage occurred, followed by a severe systemic reaction and high temperature but no localized infection or necrosis resulted.

A few cases with small angiomata in the mucosa of the mouth were effectively treated by the implantation of one or more gold radon seeds using 0.3 to 0.5 mc. per cc. of angiomatous tissue; the response was very gratifying.

ANALYSIS OF OUR CASES

A survey of our clinical material permits of certain deductions. In Table I the distribution of the patients as to age, sex and type of lesion is given. The classification of MacKee described in the introduction has been used, indicating by S (superficial) the strawberry mark, D (deep) the cavernous angioma. In addition to the 146 hemangiomata there were 4 portwine marks, 1 lymphangioma and 1 nevus pilosus. The ratio between males and females is 1 to 2, which agrees with MacCollum's[12] and Andren's[1] figures, while Müller[14] found it to be 1 to 3. The majority of our patients were referred for treatment during the first year of life with a definite peak during the age period of two to six months. About 40 per cent of the lesions were found on the face and neck. Over 10 per cent had multiple angiomata, and the highest number of lesions in one child was 7 (Table II).

A review of the records revealed also the following information: The shortest treatment period was one month, the shortest observation period three months; the longest treatment period was two years three

TABLE II

LOCATION OF NEVI

Age	Scalp	Face and Neck	Trunk	Extremities	Multiple
0– 2 mo.	5	—	—	2	1* (7)
2– 6 mo.	13	20	7	19	6 (2) 1 (3)
6–12 mo.	9	18	8	7	4 (2)
1– 3 yr.	2	9	7	2	4 (2) 1 (3)
3–10 yr.	—	4	1	1	—
Over 10 yr.	1	11	—	6	—
	30	62	23	37	

* The figures in parentheses refer to the number of the lesions found in the same patient.

months, the longest observation period was seven years. The smallest total dose with the plaque only was 10 mg-hr., the largest 55 mg-hr.; the smallest total dose with screens only 100 mc-hr., the largest 1,500 mc-hr. The smallest total dose with the combined treatment (plaque and screens) was 6 mg-hr. and 100 mc-hr. respectively, the largest 10 mg-hr. and 1,300 mc-hr. The average treatment period was nine months and the average observation period was 25.8 months.

The evaluation of the end-results obtained in our series is limited to 146 vascular and cavernous hemangiomata. We classified as "excellent" those where the site of the angioma could not be detected, as "satisfactory" those where some scarring or discoloration remained, as "failure" those which did not respond at all, as "incomplete" those who did not return for observation after their last treatment and as "under treatment" those who might still require additional therapy. According to the figures compiled in Table III, approximately 60 per cent of our cases were definitely cured, although at least one-half of those termed "incomplete" can be considered in the same category. Our hospital receives a little over 90 per cent charity patients, and we know from experience that parents are apt to forget their appointments for re-examination of the child just as soon as they are satisfied with the cosmetic result. We have many letters to that effect in our files. Yet, only patients re-examined by us were included in columns 2 and 3 of Table III. The percentage of actual failures is very small; in our series it amounted to only 2.2 per cent.

Table III

RESULTS IN 146 HEMANGIOMATA

Age	Excellent*	Satisfactory	Failure	Incomplete	Under Rx	Total
0– 2 mo.	— (1)	2 (—)	— (1)	— (2)	1	3 (4)
2– 6 mo.	15 (3)	15 (4)	— (1)	11 (3)	4 (3)	45 (14)
6–12 mo.	7 (6)	6 (4)	— (—)	2 (7)	2 (5)	17 (22)
1– 3 yr.	2 (2)	2 (4)	— (—)	1 (2)	2 (5)	7 (13)
3–10 yr.	1 (—)	1 (1)	— (—)	1 (1)	1 (—)	4 (2)
Over 10 yr.	3 (1)	2 (4)	— (1)	2 (2)	— (—)	7 (8)
	28 (13)	28 (17)	— (3)	17 (17)	10 (13)	83 (63)
	28.2%	30.7%	2.2%	23.2%	15.7%	146

* The figures in parentheses refer to deep, the others to superficial lesions.

COMMENT

A comparison of the results of radium therapy obtained in our series with those recorded in the literature shows that some authors give higher figures varying from 73 per cent[4] to over 90 per cent.[3,6,21] An analysis of the statistics published during the last ten years leads us to believe that a complete cure may reasonably be expected in approximately 75 per cent without such late injuries as atrophy or telangiectasis, provided the conservative method practiced by us and described by Andren[1] as the "expectant method of Forssell" is employed. According to Baensch[6] the interstitial use of radium needles produces good results in "practically all cases" so that he considers it the method of choice. However, it requires hospitalization for at least three days and there is also the danger—even if slight—of hemorrhage and secondary infection. On the other hand, the disadvantage of the conservative approach lies in the difficulty of inducing the parents to bring the child to the clinic repeatedly for treatment and observation over an average period of almost a year. If the new method described by Strandqvist,[21] which assures satisfactory results in 94 per cent of uncomplicated cases with one single radium appli-

cation, can be confirmed by others, then, indeed, has definite progress been made in the treatment of vascular nevi by means of radium surface applicators.

SUMMARY

1. The classification, etiology and histology of vascular nevi are briefly described; their treatment early in life is indicated since spontaneous cures are rare.

2. The various treatment methods are mentioned and the technique of radium therapy is outlined in detail.

3. One hundred forty-six cases of hemangioma treated during the last decade in the Department of Radiology of the State of Wisconsin General Hospital in Madison are reported and analyzed. Statistics regarding the distribution of these nevi as to age, sex, type and location. as well as the end-results obtained are presented.

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* No attempt has been made to record all papers published on this subject.

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DISCUSSION

Dr. Edward H. Skinner, Kansas City, Mo. It is easy to agree with the various points in Dr. Pohle's presentation. I should like to offer a few observations which have developed out of a long experience with reference to the appearance of patients who have had cavernous angiomas and who have been seen from twenty to twenty-five years following the radiation treatment. I also want to suggest two other methods of treatment.

One method is similar to the tray method to which Dr. Pohle referred as the Stockholm method. The radium needles are held in a brass tray of appropriate size in an arrangement favorable for homogeneous irradiation by paraffin. This tray is covered with rubber tire stock. A handle is attached, usually a tongue depressor, and the mother irons the area. This is particularly useful in some lesions within the mouth where both you and the parents wish to avoid the insertion of needles or radon implants.

Another tray method is useful in hemangiomas of the tongue, which frequently have a concomitant lymphangioma. For these patients we make the surface radium applicator up so that it resembles a lollypop.

The one thing that is necessary is patience in the care of these little ones. You must not try to do too much at once. Frequently, we discuss the situation with the parents upon the idea that it may be one or two years before we attain the maximum result, re-treating the patient at intervals of from three to four months. That seems essential, if you hope to avoid too much scarring.

One method of treatment which is very simple and useful, especially in the large cavernous hemangiomas around the neck where in treating these you would get a good deal of cross-fire, is the injection of boiling water. It is an old method and is described in Binnie's classical "Operative Surgery." After the needle is inserted you are assured by the withdrawal of the plunger that you are not in a vein and then you inject boiling water. You must protect your own hands with several pairs of sterilized, ten cent store, cotton gloves. It is a practical method and it is very useful in these larger, cavernous hemangiomas. Be sure to get the boiling water into the stroma and be sure that you are not injecting into a vein.

As to the late effects of radiation treatment upon lesions about the eyes or the nasal bones. When such cases are treated in early life and before anatomical development is complete, you may have some facial asymmetry in adult life. These cases do not lend themselves to the hot water injection or to radon implants or to any method by which you are likely to get an embolus or to have an infection extending into the cranial cavity. While the use of the surface applicator here will reduce the cavernous hemangiomas, there will be some deformity of that side of the nose as a sequela.

I remember the first case of this type that was sent to me by an equine and vehicular surgeon from Halstead who did not wish to inject hot water or use the actual cautery and insisted that I should complete the job by irradiation. This was done more than twenty-six years ago. I see the patient occasionally, and she has a very beautiful face on one side but quite a concavity on the side of the nose where this large hemangioma projected at the inner canthus.

There are some interesting situations that become individual to the given case, and it requires a good deal of ingenuity at times to develop an applicator which is satisfactory. I am not at all addicted to the use of needles, because as Dr. Pohle has said, hospitalization is necessary; they are very difficult to keep in position, and they are not at all readily accepted by the patient or the parents. Even these huge lesions of the arm, such as Dr. Pohle shows in his exhibit, are readily taken care of by surface applications, if you take the time.

THE EFFECT OF ROENTGEN IRRADIATION ON THE LYMPHATIC TRANSPORT OF INDIA INK

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FOR many years the objection has occasionally been raised, more often verbally than in writing, that irradiation appears to be responsible in some cases for widespread dissemination of cancer cells. As recently as 1932 an editorial[1] appeared in the *American Journal of Cancer* attempting to refute such a view. It was reasoned that the explanation probably lay in the fact that treated cancer patients frequently outlive the untreated cases and that subclinical metastases in the treated patients are thereby given additional time in which to make known their presence. Granting the likelihood of such a statement, it nevertheless fails to explain those instances in which rapidly advancing metastases develop either during or shortly following the course of treatment. Such occurrences are admittedly uncommon but when seen are apt to be extremely impressive. Several case reports will serve as illustration.

CASE I. A white female, aged fifty-one, arrived at the clinic on August 12, 1938, complaining of bloody nasal discharge and impaired hearing on the right of two months' duration. On examination a tumor, 2 cm. in diameter, was found in the right fossa of Rosenmüller. There were no palpable cervical nodes and the remainder of the examination was unremarkable. A nasopharynx biopsy was reported as showing epidermoid carcinoma, Grade 3. Roentgen treatment was begun through two circular malar ports. Ten days later (August 23) a node was noted in the right upper neck and another in the right posterior cervical triangle. These were proved to contain metastatic disease by aspiration biopsy and were treated by the insertion of gold filtered radon seeds. Two weeks following this (September 6) a node was found in the left upper neck which was proved and treated in the same manner. Roentgen treatment to the primary growth, which was regressing satisfactorily, was completed on September 13, 1938. A nasopharyngeal applicator containing radon seeds was then inserted. All disease in the primary tumor and neck disappeared. The last note affirming this was written on December 15, 1938. The patient died on February 8, 1939, and is reported to have had metastases to the "stomach and brain."

CASE II. This case is a female, aged thirty-two, who stated that a slowly growing painless mass had been noticed in the right submaxillary region for six months. General health had been good. Past history was unremarkable. Examination revealed a rather bulky firm mass extending from the right submental area to behind the right jaw angle. There was no ulceration within the mouth, cervical adenopathy or other evidence of disease. Several aspiration biopsies yielded inadequate material for diagnosis. Fractionated roentgen treatments were given to the submental and submaxillary regions between June 4 and July 15, 1937. Regression was very rapid. On the day treatment was completed a group of nodes was noted in the right supraclavicular space and another solitary node was felt in the mid neck. Aspiration biopsy of one of the right supraclavicular nodes was reported to be reticulum cell lymphosarcoma. The above mentioned nodes were treated by local roentgen irradiation and promptly regressed. On August 3, 1937, a mass was palpable in the right lower abdominal quadrant and on August 23 the patient developed a right hydrothorax. Chest roentgenograms showed mediastinal widening and infiltration of the right lower lobe. She was then given whole body irradiation on September 30, 1937, without improvement and died shortly afterward. At autopsy generalized lymphosarcomatosis was found with involvement of all lymphatic node groups, most of the abdominal organs and all serous membranes.

CASE III. Male, aged sixty, complaining of sore throat of nine weeks' duration. On examination he was found to have a carcinoma (epidermoid Grade 2) involving the left arytenoid and aryepiglottic fold. No enlarged neck nodes were palpable on admission. The tumor was treated by roentgen radiation crossfiring through

two portals, one to either side of the neck. This was followed by complete regression. One month following treatment a node was noted beneath the sternomastoid muscle in the left mid neck and others rapidly developed in the left supraclavicular fossa. The patient's condition grew steadily worse and death ensued three months after treatment to the larynx was completed. At autopsy additional metastases were found in the mediastinum, lungs and liver.

It is probable and is commonly taken for granted that malignant cells were already present in these extra-primary sites and that their assumption of clinical significance was merely coincident with the treatment. Inasmuch as this is a point which by present clinical or laboratory methods it is impossible either to establish or disprove, it becomes obligatory to determine whether certain changes known to be produced by irradiation might or might not account for the phenomenon before such happenings can be thus summarily disposed of.

It is well known that when tissue has been sufficiently exposed to roentgen rays or gamma rays certain changes take place, usually within ten to fourteen days, which together are spoken of as an "initial" reaction. Macroscopically this appears in the form of local redness and an increase in local heat with some swelling. The attendant microscopic picture is one of cellular edema, leukocytic infiltration and vascular engorgement. During this period which generally lasts about two weeks, many cells disintegrate. In others, less severely injured, the changes seem to be reversible, for a return to their pre-irradiation histologic state follows. Apparently all cells of whatever nature react in a similar manner though to a variable degree, cancer cells in general being more sensitive than those of their parent tissue or of the tumor stroma.

Normal lymphatics constitute a closed system and malignant cells are able to enter only after the continuity of the endothelial wall has been disrupted. This injury is ordinarily accomplished by direct penetration of the advancing tumor cells. If, therefore, an earlier and more rapid lymphatic spread of cancer cells were produced by irradiation or any other means, it is probable that either of two mechanisms or possibly both are responsible, namely injury to the capillary walls and an increased lymph flow. Knowing the effect of irradiation on tissue, it is not inconceivable that during the acute reaction phase some damage to the endothelial cells of the lymphatics might occur, producing fenestrations in an otherwise closed system through which unsterilized tumor cells dislodged by surrounding edema and cellular breakdown, and aided by normal movements of the parts could now pass unhindered. Neither would it be difficult to imagine, in view of the observable redness and engorgement characteristic of the reaction period, that a local increase in the velocity of lymph flow might occur. The following study was undertaken to ascertain the validity of these two hypotheses.

EXPERIMENTAL

It was reasoned that if some non-irritating, readily demonstrable particulate matter which would rapidly be ingested by phagocytes were injected, the course of the particle containing phagocytic cells from the site of injection through the lymphatics could easily be detected and a quantitative estimate made of the number of cells entering and traversing these vessels. Any altering effect produced by irradiation could also be determined. Since carbon particles are chemically inert, are easily visible grossly and microscopically, and are quickly taken up by the macrophages in which they eventually are carried into the lymphatics, it appeared that this sort of material provided a suitable indicator of lymphatic permeability and rate of lymph flow for the present purpose.

Procedure. Higgins American India ink (black) was used, diluted with distilled water in the proportions of 1:25 and 1:50. The solutions were sterilized in a steam autoclave at 15 pounds pressure for fifteen minutes; 0.25 cc. of the diluted pigment was injected subcutaneously, using a 26 gauge needle, into both pectoral regions of healthy, young adult (three to six months old) male

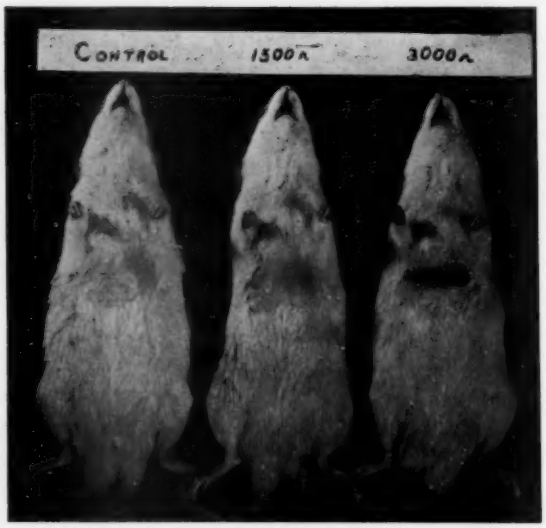

FIG. 1. Shows the slight reddening with 1,500 r and the more marked reaction and epilation with 3,000 r two weeks following irradiation. Animals treated with 1,500 r usually showed about 50 per cent epilation at three weeks.

and female albino rats, using the 1:25 dilution on the right and the 1:50 on the left.

Twenty-four hours later the animals were irradiated in the following manner: Immobilized ventral surface uppermost, they were covered by a specially constructed shield of 5 mm. of lead and 1 mm. of celluloid, the celluloid just touching the ventral hair. A rectangular, centrally placed aperture in the shield measuring 2×4 cm. exposed the sites of injection. The remainder of the animal, including the axillary nodes, was therefore largely protected from the rays.

The rats were then placed directly under the target of a roentgen tube at a distance of 50 cm. from its target (target skin distance) and given doses (as measured in air) of 750 r, 1,500 r or 3,000 r each. The tube used was one of the standard water-cooled Coolidge type operated under the following physical conditions: 200 kv. and 30 ma., with 0.50 mm. copper and 1.6 mm. aluminum filter. This setup produced a radiation intensity of 56 r per minute.

A control group of animals was injected with the ink but received no irradiation.

Within two to four weeks following injection and irradiation the animals were killed. A careful dissection of axillary and mediastinal nodes was done and these were then sectioned serially and stained with hematoxylin and eosin.

Results. The course taken by the pigment containing cells from the site of injection in the pectoral region was always to the axillary nodes which lie in a chain beneath the lateral border of the pectoral muscles and thence to the upper anterior mediastinal nodes. (The rat has no nodes corresponding anatomically to the supraclavicular group in man.) No gross pigment was ever noted in the inguinal nodes, liver or spleen.

A preliminary study of non-irradiated animals killed at daily intervals following ink injection had shown that within twenty-four hours a fair proportion of the carbon particles had already been phagocyted and after several days most of the ink had been taken up, some of the macrophages ap-

FIG. 2. Indicates the axillary lymph nodes, several of which are seen to be filled with the carbon particles. (Control animal four weeks after injection.)

pearing almost solidly black. No quantitative difference in the number of phagocytes present at the site of injection was apparent in the control and irradiated groups of animals. It was also noted that often within twenty-four hours the axillary nodes contained a barely appreciable quantity of pigment which quite rapidly increased in amount so that at four to five days following injection it was usually easily visible grossly. This rapid appearance within the axillary nodes undoubtedly resulted from actual puncture of lymph vessels by the injecting needle and on several occasions tiny threadlike streaks were seen to radiate from the needle point toward the axilla.

Fig. 3. The sternum has been split and the anterior thoracic flaps are retracted upward showing several of the upper mediastinal nodes containing pigment. (Animal killed four weeks after receiving 1,500 r.)

Fig. 4. Shows ink granules filling many phagocytic cells. Occasional particles may still be seen lying free. (Two weeks following injection.)

Pigment was rarely found in the mediastinal nodes before two weeks had elapsed. It is certain, therefore, that by the time reaction to the irradiation appeared pigment containing cells were present both within and without the lymphatics. Visible reaction occurred only in animals receiving doses of 1,500 r and 3,000 r. It generally appeared about ten days following treatment and consisted initially of slight local reddening followed in three to five days by superficial desquamation and beginning epilation. Slight vesication was occasionally noted but in no instance did skin ulceration or infection develop. In those receiving 3,000 r epilation was generally complete three weeks after irradiation, but in the rats given 1,500 r only about 50 per cent epilation occurred. No hair loss was noted in animals given 750 r. Healing was complete in three and one-half to four weeks.

In addition to these skin changes there

FIG. 5. Lymph node showing many pigment containing cells. (Eosin stain for better contrast and therefore cell nuclei are not seen.)

was noted increased redness and some edema of the anterior chest muscles which on microscopic section appeared to have lost some of their myofibrillar striations. Subpleural petechial hemorrhages were sometimes seen in animals which had received 3,000 r. Several animals which developed pneumonia were discarded.

A constitutional effect as evidenced by weight loss was observed in those given 3,000 r. This loss averaged 15–25 per cent of their original weight. The animals given 750 r and 1,500 r generally continued to gain weight more or less commensurate with their age and size at the time of injection.

Pigment was usually grossly visible in the nodes which appeared gray or black in color, depending on the amount contained. One could not be certain of any consistent quantitative difference in the node deposits of the irradiated and non-irradiated animals on gross examination. On grading the microscopic sections, however, it became obvious in comparing averages that the axillary nodes of the irradiated animals in which visible reaction had been produced certainly contained no more pigment than did those of the non-irradiated group. Instead they seemed to contain a slightly lesser amount as is shown in Table 1. The same appeared to be true of the mediastinal nodes. The nodes of animals killed three to four weeks after treatment were found to contain only a little more pigment than those of animals killed within the two to three week period.

DISCUSSION

Earlier the statement was made that the hypothetical possibility of irradiation producing cancer dissemination must depend on the working of either of two mechanisms or both. Assuming that the lymphatics had not already been invaded, entrance into them could only be accomplished following injury to their endothelial wall as a result of the same influences acting to destroy the tumor cells, though to a smaller degree. Cells already present within the lymphatics, however, would, in the presence of intact nodes, depend on increased velocity of lymph flow for their more rapid dissemination.

If the first of these hypotheses were true, the axillary nodes of the irradiated animals would be expected to contain more pigment filled cells than the corresponding nodes of the controls, mainly as a result of the increased number entering the lymph capillaries at the reaction site. The validity of the second would be substantiated, on the other hand, by finding a relatively greater amount of pigment in the mediastinal nodes of the irradiated animals. However, since neither node group in the treated rats contained any more pigment than did those of the controls, it seems safe to assert that both suppositions, though theoretically possible, are without factual basis. It therefore becomes difficult to understand how irradiation could be instrumental in scattering cancer cells, and it appears that one must assume by analogy that the relationship between rapidly occurring new foci of disease and irradiation in the treatment of certain cancer patients is a matter of coincidence only.

TABLE I

TABULATION OF EXPERIMENTAL DATA INDICATING THE SEVERAL GROUPS OF ANIMALS STUDIED AND THE RELATIVE AMOUNTS OF PIGMENT TRANSMITTED FROM THE SITE OF INJECTION IN EACH

Group	Axillary Nodes		Upper Mediastinal Nodes		Total Axillary Nodes	Total Upper Mediastinal Nodes
	2–3 weeks	3–4 weeks	2–3 weeks	3–4 weeks	(2–4 weeks)	(2–4 weeks)
Controls	*15 **4.4	21 4.8	10 1.9	20 2.0	36 4.63	30 2.0
750 r	9 4.9	9 4.45	4 1.5	8 1.5	18 4.67	12 1.5
1,500 r	10 3.8	8 4.1	5 1.4	8 1.88	18 3.94	13 1.69
3,000 r	10 3.2	6 3.66	4 1.5	6 1.66	16 3.38	10 1.66
1,500 r and 3,000 r	20 3.5	14 3.9	9 1.45	14 1.8	34 3.7	23 1.65

* Figures in left upper corner of boxes represent number of experimental animals.
** Represent averages obtained in grading two sets of slides from each group of nodes as to their pigment content, the slide numbers being masked at the time of grading.

Actually, as has been stated, the nodes of the irradiated animals contained quantitatively less pigment than did those of the controls. The difference was not marked but was certainly greater than that between animals killed after two to three weeks and those killed after three to four weeks. Why this occurred is not quite clear. Obliteration of the lymphatic vessels due to tissue edema might account for some of it. There is also the possibility that swelling of the macrophages, a phenomenon by no means peculiar to these cells alone, interfered mechanically with their lymphatic entry.

SUMMARY AND CONCLUSIONS

1. An attempt has been made to determine whether or not irradiation facilitates the immediate lymphatic dissemination of cells.

2. India ink was used as an indicator and the experimental method has been described.

3. The results, showing a lesser quantity of pigment in both the axillary and the mediastinal nodes of the irradiated animals as compared to those of controls, suggest that neither injury to the lymphatic vessels nor increase in lymph flow sufficient to favor cellular dissemination occurs as a result of irradiation. It therefore seems probable that metastases becoming clinically apparent during the course of radiation therapy were already present in subclinical form before treatment was begun.

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Forty-second Annual Meeting: Cincinnati, 1941.

THE AMERICAN RADIUM SOCIETY

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Committee on Arrangements: L. A. Pomeroy, Chairman, Cleveland, Ohio, J. R. Driver, Cleveland, Ohio, Harry Hauser, Cleveland, Ohio.

Representatives on American Board of Radiology: Douglas Quick, New York City, R. H. Stevens, Detroit, Mich., B. P. Widmann, Philadelphia, Pa.

Twenty-sixth Annual Meeting: Cleveland, Ohio, June 2–3, 1941.

EDITORIAL

THE ANNUAL MEETING

THE meeting of the American Roentgen Ray Society held in Boston from the first to the fourth of October, 1940, was the Forty-first Annual Meeting and it stands out as one to be long remembered. From the beginning of the Call to Order by President Edward L. Jenkinson until the final adjournment on Friday afternoon there was not a dull nor an unimportant moment. Following the Call to Order there were the presentation of Certificates of Merit awarded for scientific exhibits at the Fortieth Annual Meeting, the Address of Welcome by Dr. C. Sidney Burwell, Dean of the Medical Faculty, Harvard University, and the Installation of the President Elect Dr. Merrill C. Sosman. In his Inaugural Address Dr. Sosman discussed "Specialization in Roentgenology," a very stimulating and thought-provoking topic which is published elsewhere in this issue of the JOURNAL.

In the arrangement of the program, Dr. Sosman and his committee had grouped the clinical and physical papers in various symposia and the entire mornings were given over to these papers and discussions, with the exception of one hour from ten to eleven during which time was given to view the extensive scientific and commercial exhibits. The four afternoons were given over to special clinical lectures and to the instruction courses. These lectures were a new feature in the program arrangement and proved to be a most interesting part of the meeting.

On the afternoon of Tuesday, the first day, the special clinical lecture was given by Dr. Shields Warren of Boston on "Radiosensitivity of Tumors." He said that the varied response of different types of tumors to radiation still rests on an empirical basis, although in general the less differentiated tumors respond better than highly differentiated ones. The response depends not only on the character of the tumor itself but also on the character of the supporting tissue, the presence or absence of associated infection, and whether or not previous radiation has been given. He grouped tumors into three classes: the radiosensitive, the radioresponsive, and the radioresistant. In the response to radiation, the direct effect of the type cell of the tumor, the alteration of the connective tissue of the stroma and the injury to stromal blood vessels all play important parts. He called attention to the fact that increased radioresistance of tumors following their initial irradiation is not clearly defined but undoubtedly stromal and vascular changes play an important part. The lecture was illustrated with various types of sensitive and resistant tumors.

On Wednesday afternoon there was a most unusual and instructive clinical lecture on "X-Rays in Veterinary Medicine" by Gerry B. Schnelle, V.M.D., of Boston. This proved to be one of the most interesting sessions of the meeting. The committee had arranged this in a sort of "Information Please" type of program with Dr. Schnelle presenting various roentgenograms of animals, and these roentgenograms were discussed by "experts" Dr. S. W. Donaldson, Dr. V. W. Archer and Dr. W. E. Chamberlain. One interesting point brought out was that most of the conditions found in animals may be readily diagnosed by the similarity to roentgen findings in the human; particularly is this true in various skeletal disturbances.

On Thursday afternoon the special

clinical lecture was on "Leukemia" and was given by Dr. William B. Castle of Boston. This was a most comprehensive clinical discussion of this disease including its differential diagnosis, prognosis, treatment and care of patients, from the non-roentgenological aspect.

On the fourth afternoon the special clinical lecture was on "Osteoporosis" given by Dr. Fuller Albright of Boston. He discussed and defined the term osteoporosis. He drew schematic charts illustrating the calcium and phosphorus metabolism in the normal individual and presented schematic charts of various generalized metabolic disorders which included osteomalacia, osteitis fibrosa, Paget's disease, and osteoporosis. He discussed the clinical conditions which lead to osteoporosis, calling particular attention to post-menopausal osteoporosis and the influence of hormonal therapy on post-menopausal osteoporosis and various other phases of bone dyscrasias.

The Instruction Courses which occupied the remaining part of the afternoon sessions still proved to be very popular and undoubtedly will become a permanent feature of the annual meetings. To Dr. Kirklin who has labored so persistently and capably in the arrangement of the courses the Society owes its thanks.

On Thursday evening the annual Caldwell Lecture was given by Dr. George W. Holmes. He chose as his subject "The Development of the Science of Roentgen Technique," a topic of discussion in which Caldwell would have delighted. Dr. Holmes was very graciously introduced by Dr. Percy Brown. At the conclusion of the lecture Dr. Holmes was presented by President Sosman with the Caldwell Medal.

The Annual Banquet was held on Thursday evening, preceded by a reception given by the New England Roentgen Ray Society. Much excellent entertainment had been arranged during the dinner and immediately afterward, Professor H. E. Edgerton of the Massachusetts Institute of Technology gave a most delightful talk on the stroboscope and some of its uses. This he illustrated with beautiful black and white and color stroboscopic motion pictures. An hour of dancing closed a most satisfactory evening.

The annual golf tournament was held on Monday, the day preceding the official opening of the meeting, at the Commonwealth Country Club. This was participated in by a great number of the members of the Society and there was keen competition for the Willis F. Manges Trophy, which was won by Dr. B. R. Kirklin. For the first time an additional trophy, a beautiful silver cup, was given by the commercial manufacturers. This trophy was offered as a prize for the Kicker's Handicap and was won by Dr. Jesse R. Cooper. This cup was a very thoughtful gift on the part of the commercial exhibitors and to them the Society wishes to express its appreciation and thanks. This represents one of the many expressions of the very friendly spirit of cooperation that obtains between the manufacturers and the Society.

Boston and its vicinity, in the magnificent schools and public buildings and historic associations, lends itself splendidly to sightseeing, and the wives of the local members of the Society had organized an excellent program for the visiting ladies. This is a feature too often absent in our annual meetings and it was a happy thought on the part of the Committee on Arrangements to revive a somewhat neglected custom.

The Scientific Exhibits were splendidly housed in an adequate space accessible to the meeting rooms and to the commercial exhibits and Dr. Donaldson and his committee had arranged a comprehensive group of exhibits. A more extended review of these and the awards to the various exhibitors is given elsewhere in this issue.

The Commercial Exhibits attracted a great deal of attention and justly so because of the extensive display of modern machines and accessories. These exhibits, which surpassed in number those of any former meeting, were arranged in an ample

space and against an attractive background.

The hotel accommodations were such as to elicit nothing but praise from the members of the Society and their guests, and to the Manager of the Hotel Statler and his very efficient staff the Society wishes to express its thanks and appreciation.

To the New England Roentgen Ray Society, to Dr. Sosman and his Program Committee, and to the other committees which cooperated, the Society desires to express its grateful appreciation. The quality and character of the meeting were such that it stands out as one of the best that the Society has ever had.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY
Secretary, Dr. C. B. Peirce, Royal Victoria Hospital, Montreal, Canada. Annual Meeting: Cincinnati, Ohio, 1941.

AMERICAN COLLEGE OF RADIOLOGY
Secretary, Mac F. Cahal, 540 N. Michigan Ave., Chicago, Ill. Next annual meeting: 1941, to be announced.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
Secretary, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio. Annual meeting: Cleveland, Ohio, June 2-6, 1941.

RADIOLOGICAL SOCIETY OF NORTH AMERICA
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: Cleveland, Ohio, Dec. 2–6, 1940.

RADIOLOGICAL SECTION, BALTIMORE MEDICAL SOCIETY
Secretary, Dr. Walter L. Kilby, Baltimore. Meets third Tuesday each month, September to May.

RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY
Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets twice annually in May and September.

SECTION ON RADIOLOGY, ILLINOIS STATE MEDICAL SOCIETY
Secretary, Dr. H. W. Ackemann, 321 W. State St., Rockford, Ill.

RADIOLOGICAL SECTION, LOS ANGELES CO. MED. SOC.
Secretary, Dr. Wilbur Bailey, 2007 Wilshire Blvd., Los Angeles, Calif. Meets on second Wednesday of each month at County Society Building.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. Roy G. Giles, Temple, Texas.

BROOKLYN ROENTGEN RAY SOCIETY
Secretary, Dr. L. J. Taormina, 1093 Gates Ave., Brooklyn, N. Y. Meets monthly on fourth Tuesday, October to April.

BUFFALO RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Joseph S. Gian-Francheschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months, place of meeting selected by the host.

CHICAGO ROENTGEN SOCIETY
Secretary, Dr. C. J. Challenger, 3117 Logan Blvd. Meets second Thursday of each month October to April inclusive at the Palmer House.

CINCINNATI RADIOLOGICAL SOCIETY
Secretary, Dr. J. E. McCarthy, 707 Race St., Cincinnati, Ohio. Meets third Tuesday of each month, October to May, inclusive.

CLEVELAND RADIOLOGICAL SOCIETY
Secretary, Dr. H. A. Mahrer, 10515 Carnegie Ave. Meets at 6:30 P.M. at Mid-Day Club rooms on fourth Monday each month, October to April, inclusive.

DENVER RADIOLOGICAL CLUB
Secretary, Dr. P. R. Weeks, 520 Republic Bldg., Denver, Colo. Meets third Friday of each month.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY
Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

FLORIDA STATE RADIOLOGICAL SOCIETY
Secretary, Dr. J. N. Moore, 210 Professional Bldg., Ocala, Florida. Meetings in May and November.

GEORGIA RADIOLOGICAL SOCIETY
Secretary, Dr. R. C. Pendergrass, Prather Clinic Bldg., Americus, Ga. Meets in November and at annual meeting of Medical Association of Georgia in the spring.

ILLINOIS RADIOLOGICAL SOCIETY
Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meetings held quarterly, on the fourth Sunday of the month.

INDIANA ROENTGEN SOCIETY
Secretary, Dr. C. C. Taylor, 23 E. Ohio St., Indianapolis, Ind. Meeting held the second Sunday in May annually.

KENTUCKY RADIOLOGICAL SOCIETY
Secretary, Dr. J. C. Bell, 402 Heyburn Bldg., Louisville. Meets annually in Louisville on third Sunday afternoon in April.

LONG ISLAND RADIOLOGICAL SOCIETY
Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:30 P.M.

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS
Secretary, Dr. J. E. Lofstrom, 1536 David Whitney Bldg., Detroit. Three meetings a year, Fall, Winter, Spring.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary, Dr. I. I. Cowan, Mt. Sinai Hospital, Milwaukee, Wis. Meets monthly on first Friday at University Club.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary, Dr. J. P. Medelman, 572 Lowry Medical Arts Bldg., St. Paul.

NEBRASKA RADIOLOGICAL SOCIETY
Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month, at 6 P.M. at either Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. A. O. Hampton, Massachusetts General Hospital, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

RADIOLOGICAL SOCIETY OF NEW JERSEY
Secretary, Dr. W. J. Marquis, 198 Clinton Ave., Newark. Meets annually at time and place of State Medical Society. Mid-year meetings at place chosen by president.

NEW YORK ROENTGEN SOCIETY
Secretary, Dr. E. J. Ryan, St. Luke's Hospital, New York City. Meets monthly on third Monday, New York Academy of Medicine, at 8:00 P.M.

NORTH CAROLINA ROENTGEN RAY SOCIETY
Secretary, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

CENTRAL NEW YORK ROENTGEN RAY SOCIETY
Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse. Three meetings a year. January, May, November.

OHIO RADIOLOGICAL SOCIETY
Secretary, Dr. J. E. McCarthy, 707 Race St., Cincinnati. Meets at time and place of annual meeting of Ohio State Medical Association.

PACIFIC ROENTGEN SOCIETY
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. L. E. Wurster, 416 Pine St., Williamsport Pa. Meets annually.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. B. R. Young, Temple University Hospital. Meeting first Thursday of each month from October to May inclusive, at 8:15 P.M., in Thompson Hall, College of Physicians, 19 S. 22d St.

PITTSBURGH ROENTGEN SOCIETY
Secretary, Dr. H. W. Jacox, 4800 Friendship Ave. Meetings held second Wednesday each month, 4:30 P.M., October to June at various hospitals.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary, Dr. S. C. Davidson, 277 Alexander St. Meets on second Thursday from October to May, inclusive, 8 P.M., Rochester Academy of Medicine Building.

ST. LOUIS SOCIETY OF RADIOLOGISTS
Secretary, Dr. W. K. Mueller, University Club Bldg. Meets fourth Wednesday of October, January, March and May, at a place designated by the president.

SAN FRANCISCO RADIOLOGICAL SOCIETY
Secretary, Dr. H. A. Hill, 450 Sutter St., San Francisco. Meets monthly on third Thursday at 7:45 P.M., first six months at Toland Hall, second at Lane Hall.

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

South Carolina X-Ray Society
Secretary, Dr. T. A. Pitts, Baptist Hospital, Columbia, S. C. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

Tennessee Radiological Society
Secretary, Dr. F. B. Bogart, 311 Medical Arts Bldg., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. L. W. Baird, Scott and White Hospital, Temple, Texas. Next annual meeting, January 18, 1941, Sherman, Texas.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:00–5:00 P.M., Room 301, Service Memorial Institute.

Virginia Radiological Society
Secretary, Dr. C. H. Peterson, 603 Medical Arts Bldg., Roanoke, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. K. J. Holtz, American Bank Bldg., Seattle. Meets fourth Monday of each month at the College Club, Seattle.

Cuba

Sociedad Cubana de Radiologica y Fisioterapia
Secretary, Dr. Francisco Padron, Enrique, Villuendas 64, Havana, Cuba. Meets monthly in Havana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets monthly on third Thursday from November to June inclusive, at 8:15 P.M., 32 Welbeck St., London.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:15 P.M. at the Royal Society of Medicine, 1, Wimpole St., London, W. 1.

Faculty of Radiologists
Secretary, Dr. M. H. Jupe, 32 Welbeck St., London, W. 1, England.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to November inclusive for scientific discussion.

Canadian Association of Radiologists
Secretary, Dr. A. C. Singleton, Medical Arts Bldg., Toronto, 5, Ontario.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext., Halifax, N. S.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. Colin Anderson, Invercargill, New Zealand. Meets annually.

Continental Europe

Belgian Society of Roentgenology
Secretary, Dr. J. Boine, Avenue des Alliés, 134 ,Louvain (Belgium). Meets monthly on second Sunday at d'Egmonds Palace, Brussels, except in the summertime.

Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Société de Radiologie Médicale de France
Meets monthly on second Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse, Biel. Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiologie Médicale
Meets monthly on fourth Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Association of German Roentgenologists and Radiologists in Czecho-Slovakia
Secretary, Dr. Walter Altschul, German University, Prague, II.52.

Deutsche Röntgen-Gesellschaft (Gesellschaft für Röntgenkunde und Strahlenforschung)
Meets annually in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aertze.
Permanent Secretary, Professor Dr. Haenisch, Klopstockstrasse 10, Hamburg, Germany.

Süd- und Westdeutsche Röntgengesellschaft
Meets annually in different cities.

Nord- und Ostdeutsche Röntgengesellschaft
Meets annually in different cities.

Dutch Society of Electrology and Roentgenology
Holds two meetings a year in Amsterdam, one in the spring, and one in the fall.

Societa Italiana Radiologia Medica
Secretary, M. Ponzio, University of Turin, Prof. Turin.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banul Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly on first Monday at 8 o'clock.

Polish Society of Radiology
Secretary, Dr. Jan Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. B. Krynski, 11 Zielna St. Meets once a month except in the summertime.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets every second month except in the summertime.

Society of Medical Radiology in Sweden
Meets in Stockholm.

Society of Medical Radiology in Norway
Meets in Oslo.

Society of Medical Radiology in Denmark
Secretary, Dr. G. Biering, Copenhagen. Meets the second Wednesday of each month from October to July in Copenhagen, at 8'oclock in the State Institute of Roentgenology.

Society of Medical Radiology in Finland
Meets in Helsingfors.

Vienna Roentgen Society
Meets first Wednesday of each month, at 6:30 P.M. at Zentral-Röntgen Institut des allgemeinen Krankenhauses Alserstrasse 4.

Orient

Japan X-Ray Association
c/o Orthopedic Surgery, Tokyo Imperial University. Meets annually in April.

Kinki Roentgen-Abend Society
Director, Dr. Prof. Taiga Saito, Ogawaoike Tyoto Japan. Meets bi-monthly on third Sunday.

BULLETIN OF THE INTER-SOCIETY COMMITTEE FOR RADIOLOGY

MEDICINE AND THE PRESS

The subjects of "public relations" and "publicity" have, within recent years, been mentioned with increasing frequency when groups of physicians get together for a discussion of their profession and the social and economic problems confronting it.

The fact is that doctors of medicine have only recently begun to give thought to their relations with the public. It is perhaps understandable, therefore, that the average doctor approaches the subject with less than an expert knowledge of the meaning and the technique of "public relations." The concept of public relations is foreign, indeed it is non-existent, in the training for and practice of a profession which deals solely with the individual organism. The patient is invariably studied and treated as a distinct individual; but public relations follows an opposite process. The individual is merged into the group and the social organism is studied as a whole. One of the academic postulates in psychological sociology is that the whole is greater than the sum of its parts. Examples are legion to show that the public mind is often a radically different thing from a summation of the opinions of the individuals who make up the group.

This latter phenomenon is one which the doctor may readily observe in his own relations with the public. Rarely does he find one of his patients expressing anything but respect, confidence, and admiration for his physician. It is somewhat paradoxical to observe, however, that the public, which is made up of these very same patients, manifests something akin to hostility toward the medical profession.

Of course, medicine is not the only group interest that has been tardy in recognizing the tremendous importance of that shifting, plastic thing called the public mind. Business has long recognized the value of advertising and publicity; only lately has it grasped the concept of public relations. Within the last year the National Association of Manufacturers has begun an institutional campaign and created a national information bureau as a part of a sustained public relations program directed towards winning the confidence and esteem of the public for the manufacturer.

During the last decade, the concept of public relations has suddenly struck home in the hearts of the whole generation, and as *Fortune* has said, "The vast, ephemeral, ponderous though liquid, thing called the public mind has forced itself upon the consciousness of men."

Doctors, as a whole, have begun to appreciate the importance of public relations and to realize that the profession of medicine, itself a minority group, is dependent upon the public mind for the support of its principles. Dr. Howard W. Haggard, of Yale University, one doctor who, incidentally, has manifested an erudite understanding of public relations, says, "I am convinced that it is utterly futile for the doctor to struggle against the current of public opinion. His one hope lies in changing the direction of the current. And the only way the direction of the current can be changed is through propaganda in the interest of the medical profession."

Contrary to what many persons think, publicity is not public relations. Publicity calls attention to a person, a product, a service, or an idea. Publicity has been obtained, or has resulted, when a sensational newspaper spreads the name of some doctor all over the front page in connection with a garbled story of questionable scientific veracity.

Press agentry is not public relations. Press agentry creates circumstances which get reported in the news. In the case of the medical profession, there is no need to create circumstances, because they occur with spontaneous frequency. The question is how they should be handled after they occur.

Advertising is not public relations. Ad-

vertising creates desire for or acceptance of a person, product, service, or an idea through the use of paid space or radio time. All three—publicity, press agentry, and advertising—are utilized in the technique of public relations.

These various techniques can be applied to any one of several media. The daily newspaper, the radio, the speaker's platform, the motion picture, and other media are customarily employed in any effort to influence the opinion of the public. By far the most important, however, is the daily press. The vast majority of people in this mighty land acquire the bulk of their knowledge and unconsciously form nearly all of their opinions from their daily newspaper. It is the daily newspaper, therefore, which medicine must resort to if it wants to mold the public mind.

This desire to mold the public mind, incidentally, is devoid of any ulterior motive. Everything done to foster the cause of medicine invariably reacts to the ultimate benefit of the public. Those principles to which organized medicine subscribes and which are attacked in propaganda campaigns by certain minority groups were promulgated for the benefit of the public.

This is a fact difficult of comprehension to the average newspaperman. While other organized groups were resorting to all kinds of sly tricks in an effort to obtain publicity, it has struck the newspaperman as imponderable that the medical profession was not only making no effort to obtain publicity, but was actually obstructing his efforts to obtain facts regarding medical events which he considered as having a public interest.

This curious phenomenon was the subject of comment in a recent article by Raymond Clapper, Washington correspondent for the Scripps-Howard newspapers. He describes the enthusiastic cooperation extended by the President and other administrative heads to the press. He remarks that politicians as well as industry have found that they cannot ignore the public but must actively court its favor. "The medical profession has been negligent in this regard," he concludes.

That is putting it mildly. As a matter of fact, doctors have acquired a notorious reputation among newspapermen for manifesting an inept attitude in their relations with the press. Every reporter has his tales about difficulties encountered in running down the facts on the illness of some prominent person or in covering an important medical meeting.

Newsmen, on the other hand, are traditionally looked upon with disdain by members of the medical profession because of the familiar and frequently well-founded charge that medical news in the daily press is scientifically inaccurate and factually garbled. Every doctor has witnessed the phenomenon of "parrot journalism." An enterprising newsman picks up a story about an illness or an operation on some local citizen and, just to make it good, he describes it as a "rare malady" or a "delicate operation." This inspires a similar story in some other locality, thus starting a chain of sensational dispatches, culminating in a veritable epidemic, and proving, in the end, that the condition was not "rare" at all.

Unwarranted sensationalism and carelessness in interpretation of scientific events have likewise contributed to the disrespect of the average doctor for medical news reporting. Some essayist at a medical meeting makes the cautious statement that a superabundance of vitamin E in the diet may, in the light of future experiment, lead to the indication that it is a predisposing factor in some forms of carcinoma. Another physician on the same program might refer to the presence of vitamin E in spinach. Thereupon the astonished doctors awake next morning to find their morning newspaper screaming the headline, "Spinnach Causes Cancer, Learned Doctor Declares."

Let it be clearly understood that the fault is not entirely one-sided. Sensational distortions of true scientific facts which so frequently appear in the daily press are not

solely chargeable to shoddy journalistic practices by newspapermen; some of the fault lies with the medical profession in failing to cooperate with the press by providing it with authentic material. A newspaper reporter has no deliberate desire to publish a story that is scientifically inaccurate. He frequently does so because it is so very difficult for him to run down the true facts. He is amazed at the typical reticence of the average doctor and sometimes reaches the logical conclusion that medicine desires to hide itself behind a cloak of secrecy and esoteric mystery.

A definite and sustained program in press relations for radiology has been a subject of study by the Inter-Society for Radiology and the Commission on Public Relations of the American College of Radiology. Sufficient funds are not available to permit an ambitious or a very extensive program. As indicated in the beginning of this discussion, however, a great deal can be accomplished toward the obtaining of favorable news by doing nothing more than cooperating with and offering assistance to the representatives of the press. The Commission on Public Relations proposes to provide this cooperation and assistance. The executive secretary of the College has had considerable experience in journalism and his services can be utilized in carrying out such a program.

One of the essential requisites of a news story is its timeliness. It cannot begin with a "lead" stating that "last week," or "several days ago" something happened. If it does not begin with "today" or "yesterday," it is a feature story of the magazine type. Two opportunities are presented for news stories pertaining to radiology which provide a timely element: the publication of scientific papers in the national journals and the annual sessions of the societies. It is hoped that a program will eventually be established to take advantage of all these opportunities.

At present, the Commission on Public Relations has proposed a definite program of press relations for the annual sessions of the scientific societies, and has offered its services to these societies in executing the program. The Radiological Society of North America has accepted this offer and the Commission will assist that Society's Committee on Publicity during the forthcoming meeting at Cleveland.

In brief outline, the project will be carried out as follows:

1. The advance program of the annual meeting, containing abstracts of papers, will be studied and those offering news possibilities will be selected. To be so selected, a paper must possess two requisites: it must contain material of news interest to the public and offer a vehicle for favorable propaganda. The word propaganda is here used in its enlightened sense—educational material creating a favorable understanding of the profession of radiology and its practitioners. It should be emphasized here that a paper of outstanding scientific significance may very well offer no possibilities for publicity. It may be too technical, or it may concern a subject that cannot be adequately or safely presented in a news story for the public.

2. The manuscripts of the papers selected will be requested from the essayist and the Commission's secretary will prepare a news story therefrom. These stories will be submitted to the chairman of the Commission for careful checkup to avoid any scientific inaccuracy.

3. Mimeographed copies of these stories will be prepared for release *after* the papers have been presented at the meeting. Several will be released each day at scheduled press conferences for morning and evening papers and the wire services.

4. Reporters assigned to the meeting will be met by the Commission before the session opens and press headquarters will be maintained throughout the meeting where its members will be available to answer questions and interpret papers for newsmen. The Commission will employ a photographer to provide the newspapers with photographs.

The Commission on Public Relations will undertake this new program with circumspection. It has no desire to undertake a radical or too ambitious program in the beginning. Its chief aim during the early stages of the program will be, not to

create or encourage news stories, but to avoid the publication of inaccurate or unethical stories. This can be accomplished merely by cooperating with the press and providing it with news stories of the proper type.

One principle the Commission will follow diligently. It will make every effort to discourage the publication of news that has as its principal effect the aggrandizement of an individual. Rather, it will endeavor to utilize every news story as a means of educating the public toward a respectful understanding of the science of radiology. Its aim will be to achieve recognition of the fact that a radiologist is a clinical consultant and that his profession has contributed generously to the progress of medicine and the welfare of humanity.

Mac F. Cahal
Executive Secretary

THE SCIENTIFIC EXHIBIT

The Scientific Exhibit at the Forty-first Annual Meeting of the American Roentgen Ray Society held at Boston, October 1–4, 1940, was an unusually comprehensive and instructive one and included many new and interesting subjects. The exhibits had been arranged by a committee composed by Dr. S. W. Donaldson, Chairman, Dr. V. W. Archer and Dr. P. A. Bishop. Some idea may be gained of the extent and value of the exhibit from the following brief summary of the subjects presented:

HEAD AND NECK

An exhibit in this section entitled Craniolacuna (Lückenschadel)" was presented by Drs. George M. Wyatt and Edward C. Vogt, Boston. This summarized and illustrated the findings and conclusions derived from a study of 54 cases of craniolacuna, all but two of which occurred in patients with meningoceles.

The exhibit on "Basilar Impression (Platybasia); a Skeletal Anomaly Encroaching upon Spinal Cord and Cerebellum" by Dr. W. Edward Chamberlain, Temple University Medical School, Philadelphia, pointed out that platybasia is a bizarre developmental anomaly of the occipital bone and upper cervical spine. Many patients with this anomaly develop, frequently in later life, neurologic manifestations simulating syringomyelia or disseminated sclerosis. The diagnosis rests upon recognition of the characteristic stenosis of the foramen magnum, and cephalic bulging of the clivus and neighboring bony structures into the posterior fossa of the cranium, as demonstrated by roentgenograms. While rare, the condition is of the utmost importance because surgical intervention has removed a number of cases from the hopeless categories in which they were placed by neurologic studies. The exhibit consisted of roentgenograms and transparencies showing the methods of examination in the type of deformity incident to the lesion, together with case histories and also a bibliography on platybasia.

The exhibit on "Cranial Laminagraphy" by Drs. Cornelius G. Dyke and George Belanger, Neurological Institute, New York, consisted of roentgenographic and laminagraphic studies illustrating various types of lesions and the advantages of using the laminagraph in certain intracranial neoplasms and also the value of laminagraphic studies supplementing the ordinary or usual ventriculographic and encephalographic studies, with its particular importance in tumors about the fourth ventricle.

"Pituitary Adenomas; Effect of Roentgen Treatment" was the title of an exhibit by Dr. Merrill C. Sosman, Peter Bent Brigham Hospital, Boston, and included photographs, histology, roentgenograms and visual fields showing the different responses of the three types of pituitary adenoma, namely, chromophobe, chromophile, and basophile, to roentgen therapy.

The exhibit of Dr. George Levene, Evans Memorial, Massachusetts Memorial Hospitals, Boston, was entitled "Relation of Pituitary Function to Mental Development" and consisted of roentgenograms of

the skull illustrating the architecture of the skull and purported to show the functional activity of the anterior lobe of the hypophysis as recorded in the architecture of the skull.

"Tomography of the Larynx" by Dr. Ralph M. Caulk, Warwick Clinic, Garfield Memorial Hospital, Washington, D. C., contained a demonstration of the usefulness of tomography as an adjunct to routine lateral projection and clinical examination in neoplasms of the larynx, with a description of the apparatus and technique.

THORACIC VISCERA

The exhibit of Drs. S. G. Henderson, J. M. Hill, J. W. Fisher, and G. W. Grier, Pittsburgh, Pa., on "Diagnosis and Treatment of Enlarged Thymus" consisted of roentgenograms illustrating typical appearance of enlarged thymus, the conditions which may be confused with it and the effect of radiation treatment.

Under the title of "Tracheobronchial Tuberculosis" Dr. Lowry F. Davenport, Massachusetts General Hospital, Boston, included transparencies to show certain types of tracheobronchial tuberculosis from original roentgenograms and pathological specimens.

The exhibit of "Sarcoid Disease" by Dr. Donald S. King, Massachusetts General Hospital, Boston, was composed of a series of cases to illustrate the changes in the lymph nodes and parenchyma of the lungs. The pulmonary changes may be of a miliary or more diffuse nature. Transparencies were included to show similar changes which may be present in erythema nodosum and rheumatic fever, and also to illustrate lung changes which accompany bronchial mucous membrane involvement in sarcoid disease.

In "Bronchomycoses" Drs. William S. Wallace and Robert J. Reeves, Duke University Hospital, Durham, N. C., showed various types of bronchomycosis as found in that locality. A short history of each was given, and translite artist drawings of the various fungi as seen microscopically.

An exhibit by Dr. Barton R. Young, Temple University Hospital, Philadelphia, was entitled "The Value of Body Section Roentgenography (Planigraphy) in the Diagnosis of Tumors and Non-neoplastic Diseases of the Respiratory Tract." This consisted of ordinary and planigraphic roentgenograms of neoplasms and other disease processes in the neck and chest. By the use of the planigraph it is possible to delineate the soft tissues of the larynx very well in the coronal plane and thus a lesion can be lateralized. In addition, this procedure yields more information about the size and extent of a subglottic neoplasm than any other method of examination, including endoscopy. Some of the disease entities in the neck included in the exhibit were vocal cord paralysis due to involvement of the recurrent laryngeal nerve, acute and chronic laryngitis, benign and malignant laryngeal tumors, subglottic extension of laryngeal neoplasm and stenosis of the cervical trachea due to intrinsic and extrinsic tumors. In the chest the method is valuable for the demonstration of tumors and cavities, particularly when dense lung tissue around these lesions makes them difficult to visualize by non-planigraphic roentgenograms. There were illustrations of tuberculous cavities in the lungs that were not demonstrable by conventional roentgen methods, yet were clearly depicted by body section films. A number of other interesting disease processes were included. The superiority of body section roentgenography to demonstrate certain lesions was emphasized by comparison of roentgenograms made with and without the planigraph.

Drs. William Gregory Cole and Lewis Gregory Cole, St. Agnes Hospital and John B. Pierce Foundation, White Plains, N. Y., had an exhibit on "Unorthodox Microscopic Criteria of Pneumoconiosis and of Gastric Neoplasms: Correlation with Roentgenological Findings." This consisted of a correlation of usual roentgen findings with unusual pathological findings in pneumoconiosis; roentgenograms and

kodachrome photomicrographs of various types of pneumoconiosis. Correlation of usual roentgen findings and unaccepted pathological findings in gastric neoplasms. Roentgenograms and kodachrome photomicrographs of the lesions shown in the roentgenograms of gastric neoplasms. The value of this exhibit was tremendously enhanced by Dr. Lewis Gregory Cole's personal demonstration of the various points under discussion.

"A New Technique for the Arteriographic Study of the Abdominal Aorta and its Branches" was the title of an exhibit by Dr. Pedro L. Fariñas, Habana, Cuba. Puncturing the femoral artery at Scarpa's triangle a catheter is introduced through the iliac arteries into the aorta to reach the level of the vascular pedicle of the organ to be explored. The patient is then placed in the correct position for roentgenography, the contrast medium is injected through the catheter and a rapid Potter-Bucky film taken. By this method is obtained visualization of the abdominal aorta and its branches, especially those corresponding to the organ it is desired to explore. This exhibit was illustrated by roentgenograms of both animals and humans with a description of the technique and transparencies and photographs of instruments used in making the injections. This exhibit was awarded a Certificate of Merit.

Dr. Hugo Roesler, Temple University Medical School, Philadelphia, had an exhibit on "Heart Disease: Correlation of Roentgenological, Clinical and Pathological Findings." Each case presented a correlated study of roentgenologic, clinical, laboratory, electrocardiographic and postmortem examinations. The normal conditions as well as a great variety of diseases of the heart and great vessels were demonstrated. This exhibit was awarded a Certificate of Merit.

"Coronary Artery Occlusions and Anastomoses" by Drs. M. J. Schlesinger and Paul Zoll, Beth Israel Hospital, Boston, consisted of a new method of visualizing the coronary arteries of human hearts by injecting with multi-colored radiopaque masses and then unrolling the heart so that all the arteries are in one plane. A series of films showed occlusions, arteriosclerosis and anastomoses of arteries. This exhibit was accompanied by charts, one chart in particular calling attention to the correlation between coronary occlusion and angina pectoris as shown in 355 cases.

ALIMENTARY TRACT

The exhibit of Dr. Charles W. Perkins, Norwalk, Conn., on "Carcinoma of the Esophagus, Seventh Cervical to Gastric Cardia" was a case report. The literature does not describe so extensive an involvement and the patient living when examined. There were four illustrations with report of the case.

In the exhibit of Dr. Richard Schatzki, Massachusetts General Hospital, Boston, on "The Roentgenologic Demonstration of Varices of the Esophagus," the roentgen appearance of these varices and the clinical importance of their demonstration were shown. Technical factors were also stressed.

"Roentgen Examination with the Miller-Abbott Tube in Ileus" was the title of an exhibit by Drs. Octa C. Leigh, Ross Golden, and Paul C. Swenson, Presbyterian Hospital, New York. This dealt with the method of treating various forms of ileus by suction-deflation of the small intestine with the Miller-Abbott tube. A technique for the insertion of the tube was given and the part played by roentgen methods of examination during the procedure was outlined. The localization and the diagnosis of the nature of intestinal obstruction following the injection of barium sulphate suspension through the tube were illustrated.

Another exhibit by Drs. Paul C. Swenson and Ross Golden, Presbyterian Hospital, New York, was entitled "Neoplasms of the Small Intestine." This illustrated the roentgen manifestations of benign and malignant tumors of the small intestine including the duodenum. This was cor-

related somewhat with the previous exhibit dealing with the use of the Miller-Abbott tube.

A second exhibit on "Tumors of the Small Intestine" was presented by Drs. Harry M. Weber and B. R. Kirklin, Mayo Foundation, Rochester, Minn. This consisted of 96 transparencies of descriptive material, roentgenograms, photographs, of pathologic specimens and photomicrographs of the various types of true tumors encountered in the small intestine. The technique of conducting the roentgen examination was described briefly.

From the Crisler Clinic, Memphis, Tenn., was an exhibit by Dr. Walter W. Robinson on "Fluoroentgenography of the Gastrointestinal Tract: An Improvement in Method." Now that fluoroentgenography has become an integral part of every gastrointestinal examination the equipment must be flexible enough so that instantaneous exposures may be made of any part under fluoroscopic examination, and the unit should operate as well in the horizontal as in the vertical position. The improved method was shown with a specially devised cone which may be placed in the same position as ordinary cones in relation to the tube. This simple device may be added to any fluoroentgenographic unit. The unit contains a loading tunnel, sensitive automatic auxiliary control switch, and Lysholm grid is always assembled for instant use in making spot films, by compression or without compression.

A very extensive and beautiful exhibit was presented by Drs. John T. Murphy and C. E. Hufford, Toledo, Ohio, on "Bone Tumors." A series of both benign and malignant tumors of bone were shown. Many of the cases had had biopsy and the photomicrographs were shown. Where biopsy was not done, the roentgen findings were considered diagnostic. All of the cases have been followed for a number of years so that the clinical progress of each patient is known. Roentgenograms made at frequent intervals were shown so that the progress of each case could be studied. This exhibit of pathological conditions in bone was an attempt to correlate the clinical with the roentgenological and pathological findings. Most of the cases were followed either until death, or long enough to give reasonable assurance that correct clinical conclusions could be drawn. There were differences between the roentgen and pathological diagnosis in some of the cases. The subsequent clinical course often determined which one was correct. The clinical course seems to be the most important factor in determining the correct diagnosis. (The original diagnosis was given as it was made at the time the patient was first seen.) The original diagnoses as shown in the exhibit would probably be different in many instances had they been made with the aid of the present knowledge of both pathology and roentgenology. In some of the instances the original roentgen diagnosis was made elsewhere and the patient referred after roentgen diagnosis, as shown, had been made. Roentgenograms made at frequent intervals allow a study of the changes which occur either as the disease progresses or the condition improves. This excellent exhibit was given the highest award at this year's meeting, that of the Silver Medal.

"Roentgen Studies of the Shoulder" was the title of an exhibit by Drs. C. W. Blackett and T. R. Healy, Boston, in which roentgenograms of the shoulder made in four projections showed insertions of each of the short rotator tendons in profile and gave both anteroposterior and vertical views of the shoulder. They showed fragments torn from the tendon insertions, calcifications in the tendons and secondary changes in the humerus following injury.

Dr. Joseph S. Barr, New England Peabody Home for Crippled Children, Newton Center, Mass., presented the subject of "Tuberculosis of the Hip in Children." There is no constant and characteristic roentgen appearance of this condition. The disease varies markedly in the speed of its evolution. Serial roentgenograms of cases followed for as long as twenty years were

shown together with the correlated clinical data.

Dr. Fuller Albright, Massachusetts General Hospital, Boston, presented three exhibits on pathological conditions in bone. The first was entitled "Bone Changes in Post-menopausal Osteoporosis." By definition osteoporosis is a condition where the decreased bone density is due to a failure of the osteoblasts to lay down bone matrix. It is to be distinguished from conditions where lack of bone is due to an increased bone destruction or to a failure of calcium to be deposited in the matrix. The commonest form of the condition is that which occurs in women after the menopause. There it involves the spine predominantly and to a lesser degree the pelvis. The skull is seldom involved at all. Evidence that the condition responds to estrin therapy was shown.

The second exhibit of Dr. Albright's was "Osteoporosis with Cushing's Syndrome." Cushing's syndrome was carefully defined. The same type of osteoporosis is encountered as in post-menopausal osteoporosis only to a much more severe degree. The mechanism of the causation of this was demonstrated and therapeutic measures which alleviate the condition were also shown.

The third exhibit was entitled "Syndrome Characterized by Precocious Puberty When It Occurs in Females, Osteitis Fibrosis, Disseminata, Areas of Brown Pigmentation." This interesting condition is often confused with hyperparathyroidism, although it has a perfectly characteristic roentgen appearance, which should make the diagnosis easy. Some classical examples of the condition were demonstrated. For these very instructive and excellent exhibits Dr. Albright was awarded a Certificate of Merit.

Dr. Karl Kornblum, Jefferson Hospital, Philadelphia, presented the subject of "Polyostotic Fibrous Dysplasia." This is one of a group of bone conditions characterized by osteitis fibrosa. Most of these conditions present a similar roentgen appearance. It is important that the roentgenologist familiarize himself with the differential diagnosis so that he may intelligently direct the clinician in the routine investigation of cases presenting an appearance of osteitis fibrosa. This exhibit directed attention to the various conditions in this category of bone diseases with special emphasis on polyostotic fibrous dysplasia and consisted of films illustrating the distribution of the lesions throughout the skeleton with clinical comments on the various cases, and also low power photomicrographs.

An exhibit was presented on "Degenerative Changes in Joints Resulting from Continued Trauma and Increasing Age and Their Relationship to Hypertrophic Arthritis" by Drs. Walter Bauer and Granville A. Bennett, Departments of Medicine and Pathology, Harvard Medical School and the Medical Clinic, Massachusetts General Hospital, Boston. This consisted of ten charts, composed of photographs of roentgenograms, gross specimens and microscopic sections. These photographs were arranged in chronological order. They were accompanied by explanatory legends and each section was briefly summarized. The material illustrated concerned the repair of articular cartilage, the effects of patellar displacement, together with changes resulting from unusual and continued trauma. A final section was devoted to joint changes resulting from increasing age in humans.

An exhibit on "Gout" by Dr. John H. Talbott, Massachusetts General Hospital, Boston, showed roentgen changes in bones and joints of gouty patients, in various stages of the malady. Other conditions were shown which have roentgen changes similar to those seen in gout. This exhibit was beautifully illustrated with transparencies in color and by many roentgenograms showing the lesions, and photographs of pathological specimens.

An exhibit on "Classification of Tumors of the Thyroid" by Drs. Shields Warren and Hugh F. Hare, Deaconess Hospital and Lahey Clinic, Boston, consisted of a

chart showing histologic classification of thyroid tumors together with photographs of gross and microscopic specimens.

THERAPY

Two very extensive exhibits by Dr. Gordon E. Richards, Toronto General Hospital, Toronto, Canada, were entitled "Radiological Treatment of Cancer of the Tongue" and "Cancer of the Larynx." The former consisted of beautiful drawings in color of 105 cases of cancer of the tongue showing the various type of lesions and regression of the disease under treatment. In the latter were diagrammatic drawings of cases of laryngeal cancer with records of method of treatment used and result in each case. These two exhibits were awarded the Bronze Medal.

In an exhibit by Dr. Hugh F. Hare, Lahey Clinic, Boston, on "Carcinoma of the Thyroid" were given the classification and results of treatment in this condition.

"Neuroblastoma" was the title of an exhibit by Drs. George M. Wyatt and Sidney Farber, Children's Hospital, Boston, and represented a roentgen study of 44 cases of neuroblastoma seen at the Children's Hospital. Selected roentgenograms, photographs of gross specimens, and photomicrographs of primary tumors and metastases were accompanied by legends and an explanatory text. This exhibit was awarded a Certificate of Merit.

An exhibit entitled "Experimental Production of Brain Damage by Radiation" was presented by K. E. Corrigan, Ph.D., Henrietta Hayden, Ph.D., A. Derbyshire, Ph.D., and Dr. L. Reynolds, Harper Hospital, Detroit. This consisted of transparencies showing the method of operating and irradiating, clinical history, necropsy findings, histological findings including new observations in polarized light, brain wave records and artificial production of epilepsy in representative members of a series of 31 dogs. In addition it was accompanied by a motion picture in color of the dogs before and after radiation therapy showing the muscular disability and also the convulsive seizures which come following irradiation. This exhibit was awarded a Certificate of Merit.

An exhibit on "Million Volt Roentgen Rays" by Elizabeth F. Focht and Edith H. Quimby, M.S., Sc.D., Memorial Hospital, New York, comprised photographs of the 1,000 kv. installation at the Memorial Hospital during assembly and upon completion. Experimental data were given consisting of absorption curves, backscatter and depth dose curves, and comparison with doses from 200 kv. roentgen rays.

Dr. Richard Dresser and John Trump, Sc.D., Massachusetts Institute of Technology and Collis P. Huntington Hospital, Boston, in an exhibit on "Supervoltage Roentgen Rays" showed the development, by models and charts, of apparatus for the production of superhard roentgen rays using the electrostatic belt conveyor principle. Clinical and physical data were also presented.

An exhibit on "Roentgen Treatment of Gas Gangrene, Acute Peritonitis and Other Infections" by Drs. D. Arnold Dowell and James F. Kelly, School of Medicine, Creighton University, Omaha, Nebr., presented case reports and statistics which seemed to prove that roentgen therapy will prevent and cure gas gangrene without the aid of any major surgical procedure or the use of serum. The value of the mobile therapy unit in treating acute peritonitis and surgical mumps and other complications was also discussed.

"Radiation Therapy of Chronic Sinus Disease in Children" was the title of an exhibit by Dr. J. M. Dell, Jr., Gainesville, Florida, and consisted of 30 cases of chronic sinus disease in infants and children with films before and after treatment. A short legend accompanied each case. These 30 cases were selected and were representative of the results obtained in a group of some 80 infants and children.

MISCELLANEOUS

An exhibit on "Scattered Radiation un-

der Actual Conditions" was presented by Dr. Robert B. Taft, Charleston, S. C. This showed by photographs and legends the number of roentgens received by radiologist or technician in all places in and around the roentgen department. While exact conditions will not be exactly duplicated in any other laboratory, certain standard conditions will prevail from which reasonable conclusions can be drawn.

"Calcification of Ductus Deferens" was the title of an exhibit by Drs. Donald P. Ham and Joseph H. Marks, New England Deaconess Hospital, Boston. Eight cases of this condition have now been found, several of which have been proved by histological examination. Representative films, photomicrographs and anatomical charts were shown as well as other films showing arterial calcifications which can be differentiated.

"A Method of Estimating the Size of the Prostate Gland" was presented by Drs. Edward L. Pierson and Stanley A. Wilson, Salem Hospital, Salem, Mass. This was a roentgenological method of estimating the size of the gland and the degree of intravesical encroachment, and consisted in the use of the Foley catheter and a balloon in the rectum filled with sodium iodide solution.

The final exhibit was entitled "Roentgen Ray in Pregnancy" by William Snow, Bronx Hospital and Harlem Hospital, New York. This was a practical study of the size and shape of the pelvic inlet, mid pelvis and outlet correlated with the size of the fetus, based on a study of 1,100 cases. It included experimental and clinical studies of the soft tissues of pregnancy including hydramnios, normal location of the placenta, lower uterine segment, placenta previa, placental apoplexy and abdominal pregnancy.

THE COMMERCIAL EXHIBIT

The Commercial Exhibit at the Forty-first Annual Meeting of the American Roentgen Ray Society held at Boston, October 1–4, 1940, surpassed in quality and quantity any of the previous exhibits. This is a source of great satisfaction to those responsible for its arrangement. An adequate and attractive room was assigned to these exhibits and the backgrounds furnished by the Hotel in some cases and by the various manufacturers in others were designed to set off and display the beautiful and modern roentgenological equipment and the other exhibits to the best advantage. The Society is appreciative of the cooperation of the manufacturers in making available the latest designs in roentgenological equipment so that they can be seen with a minimum of effort on the part of roentgenologists. The following manufacturers were represented at the Boston meeting: *Agfa Ansco*, Binghamton, N. Y., *Buck X-Ograph Co.*, St. Louis, Mo., *Campbell X-Ray Corp.*, Boston, Mass., *Davies, Rose & Co.*, Boston, Mass., *DuPont Film Manufacturing Corp.*, New York City, *Eastman Kodak Co.*, Rochester, N. Y., *General Electric X-Ray Corp.*, Chicago, Ill., *Kelley-Koett Manufacturing Co.*, Covington, Kentucky, *Lea & Febiger*, Philadelphia, Pa., *Liebel-Flarsheim Co.*, Cincinnati, Ohio, *Machlett Laboratories*, Springdale, Conn., *National Synthetics*, New York City, *H. B. Odmann*, Little Ferry, N. J., *Patterson Screen Co.*, Towanda, Pa., *Philips Metalix Corp.*, New York City, *Picker X-Ray Corp.*, New York City, *Schering Corp.*, Bloomfield, N. J., *Frank Scholz*, Boston, Mass., *Standard X-Ray Co.*, Chicago, Ill., *Dr. L. J. Strobino*, Bethel, Conn., *Charles C Thomas*, Springfield, Ill., *Victoreen Instrument Co.*, Cleveland, Ohio, *Westinghouse X-Ray Co.*, Long Island City, N. Y., *Winthrop Chemical Co.*, New York City.

CONFERENCE OF EASTERN RADIOLOGISTS

The Thirty-first Annual Midwinter Conference of Eastern Radiologists will meet in Baltimore, Maryland, on January 31 and February 1, 1941.

DEPARTMENT OF TECHNIQUE

Department Editor: Robert B. Taft, M.D., B.S., M.A., 105 Rutledge Ave., Charleston, S. C.

ROENTGENOGRAPHIC EXAMINATION OF THE ANTERIOR PORTION OF THE EYEBALL FOR FOREIGN BODY*

By MERTHYN A. THOMAS, M.D.
CLEVELAND, OHIO

SMALL or relatively non-opaque foreign bodies in the anterior portion of the eyeball may be invisible in the lateral roentgenograms which are made as a routine in the examination of the eye for foreign bodies. This is due to the fact that the shadows of the nasal bones and orbital walls which are superimposed over this portion of the eyeball may be of equal or greater density than the foreign body. Furthermore, the region of the anterior portion of the eyeball is often so overexposed that faint shadows are completely obscured. To overcome the possibility of error from these sources, we have added to our routine lateral views a special view which permits soft tissue study of a considerable portion of the anterior part of the eyeball free from any overlying bone shadows.

Fig. 1. Shows rotation of the head from the horizontal plane and angle of the central ray.

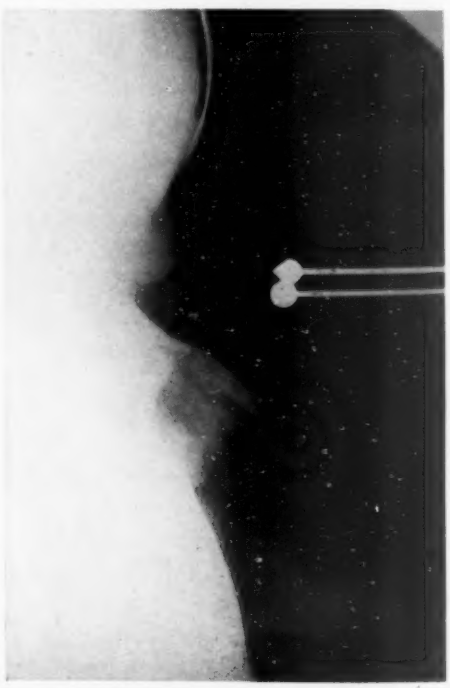

Fig. 2. Shows soft tissues of eyelids and anterior portion of the eyeball. A small foreign body is seen in the cornea opposite the arrow.

* From the Radiologic Clinic of Drs. Hill, Thomas, Farmer, Sackett, and Schumacher.

The manner in which this roentgenogram is made is as follows (Fig. 1): The patient lies on the affected side, the head resting on a low examining table. The head is rotated upward until the notch at the base of the nose and the outer wall of the orbit of the injured eye are in a plane vertical to the table. The central ray is directed along this plane in a slight cephalad-caudad direction pointing through the notch at the base of the nose toward and tangential to the surface of the eyeball. The exposure is such as will show soft tissue detail.

If a foreign body is found, localization films can be made by the Sweet method, keeping the head tilted in the same manner but being careful to maintain the usual relationship between the lines of vision and the rods of the localizer.

A film made in the above manner (Fig. 2) shows clearly a small metallic foreign body, which could not be seen in the routine lateral views nor in a posteroanterior view. This foreign body, in spite of its superficial location, could not be seen by careful physical examination and its presence was unsuspected by two ophthalmologists who had been consulted by the patient during the two months which had elapsed between the date of injury and the roentgenological examination. A third ophthalmologist requested an "x-ray examination just to rule out the presence of a foreign body."

It was localized by the Sweet method, with the head held in the tilted position as above described. At operation it was found deep in the cornea with a part of it protruding into the anterior chamber.

This method of examination is of particular value in the detection of small particles of glass. In one case we were able to localize a very tiny fragment of glass which entered the anterior chamber of the eye as the result of an explosion of an electric light bulb.

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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

HEAD

Santagati, Francesco. Anatomia radiografica dei solchi e dei canali vascolari del cranio. (Roentgen anatomy of the sulci and vessel channels of the skull.) *Radiol. med.*, April, 1939, *26*, 317–330.

The roentgen study of the anatomy of the sulci and blood vessel channels is very important from the point of view of both diagnosis and legal medicine. It also gives the surgeon valuable information in regard to routes of operation on the skull. It is difficult in view of the fact that in the skull many layers of bone are superposed and the lines of the vessels and sulci run in different planes with different angles of inclination to the plane of the projection.

In view of its importance, however, the author has made such a study and gives his results here both in the text and in roentgenograms. He discusses the individual vessels and sulci of the three systems—that of the brain tissue itself, of the bones and meninges and of the overlying soft tissues. He has determined some differential points between the various arterial and venous sulci of the skull; he believes it possible to differentiate these various vessels from each other and from pathological structures. In fact, this study is only a preliminary to a study of the roentgen diagnosis of fractures of the skull. The differentiation between vessel sulci and fracture lines is very important and not always easy—*Audrey G. Morgan.*

Santagati, Francesco. L'indagine radiologica nelle fratture della volta del cranio. (Roentgen examination in fractures of the vault of the skull.) *Radiol. med.*, June, 1939, *26*, 506–524.

The author examined the macerated skulls in the collection of the Museum of the Institute of Legal Medicine at the University of Milan for the purpose of determining the roentgen appearance of fractures of the vault of the skull; he also studied numerous roentgenograms of injured skulls in the Archives of the Roentgen Service of the Military Hospital of Milan. He found that in many cases with clinical signs of fracture of the skull roentgen examination showed a fracture. In other cases with few or no clinical symptoms roentgen examination also showed fracture. Also in some cases with manifest clinical symptoms roentgen examination did not show fracture.

While there are roentgen signs which help to differentiate between fracture and normal anatomical structures, it is also true that the roentgen images of the latter under some conditions may simulate fracture to such an extent that differentiation is very difficult. When it comes to settling medicolegal questions, a negative roentgen examination is not sufficient to exclude fracture. It is difficult to demonstrate capillary fissures on the roentgenogram, only one table may be fractured, it may not be possible to demonstrate fractures that run obliquely, especially if they are imbricated, even with tangential roentgenography. For all these reasons too much importance should not be attributed to a negative roentgen examination if there are marked clinical signs of fracture, especially if all the technical details have not been observed in making the roentgenogram. For instance, in addition to the classical projections special oblique projections should be used adapted to the different parts of the skull.

Roentgen examination should be used, however, in every case of injury of the skull as a supplement to clinical examination, particularly for the purpose of locating the fracture accurately and determining its extent and the treatment to be used, and with the object of demonstrating fractures without clinical symptoms. Such fractures are sometimes demonstrated in injuries of the skull that appear to be slight.—*Audrey G. Morgan.*

Tartagli, Dino. La diagnosi radiologica del colesteatoma. (Roentgen diagnosis of cholesteatoma.) *Radiol. med.*, April, 1939, *26*, 339–342.

At thirteen years of age the patient had a retroauricular abscess which was incised and discharged pus. From that time on he had otorrhea without any pain. He had no further manifestations until November 21, 1938, at the age of twenty-two, when he suddenly had intense

pain in the mastoid region, with headache on that side and a temperature of 38.5°. On admission to the hospital examination showed a perforation in the postero-superior quadrant of the membrane with the discharge of fetid pus.

Roentgen examination showed normal pneumatization on the left side. On the right signs of eburnation of the internal auditory canal with moderate rarefaction of the central region; below and in the cryptic section of the mastoid there was a round shadow with transparency from hyperpneumatization. It was separated from the antral region by a band of osteoid tissue slightly more opaque than the surrounding bone. A probable diagnosis of cholesteatoma was made and confirmed on operation.

The differential diagnosis between cholesteatoma and gigantic crypts, mastoid abscess and mastoid cyst is discussed.

This case differed from the usual cholesteatoma in that it was in the cryptic rather than the antral part of the mastoid. There was a focus of osteitis which had caused the pain and fever. There was also a chronic otomastoiditis of the eburnated form.—*Audrey G. Morgan.*

Casati, Annibale. La stratigrafia dei seni della faccia. (Stratigraphy of the sinuses of the face.) *Radiol. med.*, June, 1939, *26*, 546–549.

In the technique of stratigraphy the object to be examined rotates around an axis while the source of the rays remains fixed; the film may rotate or not. In either case the movement is in one direction. The table on which the object rests can be rotated at various speeds at will. The object is photographed at maximum velocity as a special interrupter makes it possible to eliminate the periods of initial and terminal slowing. The angle at which the roentgenogram can be taken is regulated at will and is always less than the angle of rotation of the table itself. By means of a special arrangement the axis of rotation may be made to pass to any desired level in the body under examination by displacing the plane of the table while the plane of rotation remains fixed. In this way an image of a series of layers may be obtained, that is, the object is sectioned roentgenographically.

This method of stratigraphy gives a very clear picture of the layer under examination and shows its structure in great detail. By making the film as well as the body to be examined rotate, the section is not thicker at the center, thinning toward the extremities, but is homogeneous and of the same thickness throughout.

With this method of stratigraphy the author studied the sinuses of the face, making serial roentgenograms of a macerated skull 1 cm. apart. The object of this study was twofold. Theoretically it was designed to make a roentgen-anatomical study of the region and practically its purpose was to make a stratigraphic analysis of the nasal route which is often followed by operators in reaching the hypophysis through the sphenoid sinus. A series of 8 roentgenograms is reproduced, showing the importance of this method of roentgen-anatomical study and giving many important details in regard to the nasal route to the hypophysis, for example demonstrating the pterygoid processes and the condition of the posterior ethmoid cells.—*Audrey G. Morgan.*

NECK AND CHEST

Vitale, Emanuele. Studio radiologico sulla insorgenza delle caverne polmonari. (Roentgen study of the development of lung cavities.) *Radiol. med.*, May, 1939, *26*, 373–394.

The development of lung cavities can be followed up by serial roentgenography from a precavernous stage to the appearance of the typical fully developed cavity. Cavities that are so small that they cannot be detected by clinical examination and very small ones deep down in the lung tissue can be detected by this means since roentgen technique has been perfected to the stage that it has reached at present.

The formation of the cavity is preceded by the development of a ring visible roentgenologically, surrounding a zone of lung tissue that is diseased but not yet broken down. The ring is made up of an infiltration of cells which demarcates the area that will later break down and form a cavity. This ring has the function of arresting the process of softening and sometimes there is a retrogression, the ring disappears and a cavity is not formed. But generally the area inside the ring goes on to necrosis.

If the process is followed up the gradual necrosis of the tissue inside the ring can be seen. The visibility of the cavity depends on its size, whether it is full or empty and whether the lung tissue around it is infiltrated and rendered more dense than normal. True cavity formation is not complete until the ichorous content has been emptied through a bronchus and the round or oval cavity is filled with air. There is then a fibrous wall around it that looks like a line drawn with pen and ink.

The serial roentgenograms should be taken at short intervals in order not to miss any steps in the process of cavity formation.—*Audrey G. Morgan.*

Gallavresi, Luigi. Metastasi pleuriche da cancro della mammella. (Pleural metastases from cancer of the breast.) *Radiol. med.*, May, 1939, *26*, 434–436.

A woman of thirty-nine was operated on in March, 1938, for carcinoma of the left breast. The breast was removed and the axilla cleaned out. She returned in January, 1939, with cough, dyspnea, pain at the base of the right lung and fever. There were physical signs of effusion of the right pleura; 2 liters of clear liquid was evacuated. In the meantime signs of recurrence in the scar and in the left axilla had appeared. Roentgen examination showed complete and uniform opacity of the right half of the thorax with dislocation of the mediastinum to the left, that is the signs of pleurisy with massive effusion. Another thoracocentesis was performed and air substituted for the liquid removed. Roentgen examination showed many polycyclic shadows along the whole lateral wall of the right half of the thorax, protruding into the cavity and showing marked contrast with the air in the cavity. These masses were evidently on the parietal pleura and beneath it. There was a sort of plate with an undulating and nodular surface extending into the right pleural sinus and along the diaphragm. The diagnosis was immense secondary neoplasm of the right pleural cavity with effusion.—*Audrey G. Morgan.*

Wallfield, Mark J. Pleural manifestations of perforation of the esophagus. *Am. J. Dis. Child.*, Dec., 1939, *58*, 1261–1264.

Wallfield reports a case of perforation of the esophagus with which was associated an esophagopleural fistula, food particles in the pleural cavity and secondary pyopneumothorax. The patient did not, however, have a diffuse suppurative mediastinitis. On thoracentesis, *B. acidophilus* was found which indicated a communication with the digestive tract. Ingestion of iodized poppyseed oil demonstrated the branching of the stream from the esophagus into the pleural cavity. In spite of both thoracotomy and gastrostomy, the patient died.—*R. S. Bromer.*

Levine, Milton I. Sequence of roentgen evidence of tuberculosis and cutaneous sensitivity to tuberculin. *Am. J. Dis. Child.*, Oct., 1939, *58*, 799–810.

Levine states that the chronologic relation between the appearance of a positive reaction to the tuberculin test and roentgen evidence of the childhood type of pulmonary tuberculosis has not yet been subjected to careful clinical investigation. He studied 63 children who contracted pulmonary tuberculosis while under one year of age and who were followed from the earliest evidence of a primary complex to calcification or death from tuberculosis. He found that 16 of these children presented roentgen evidence of pulmonary infiltration prior to the development of cutaneous sensitivity to tuberculin.

These results are contrary to the general impression now held that a positive tuberculin reaction coincides with or precedes the appearance of recognizable roentgen evidence of the early primary pulmonary complex. Levine briefly discusses the theories which may be advanced as possible explanations of his results.—*R. S. Bromer.*

Bonomini, Bruno. Osservazioni sulla destroposizione dell'arco aortico. (Observations on dextroposition of the arch of the aorta.) *Radiol. med.*, June, 1939, *26*, 525–546.

Dextroposition of the arch of the aorta is quite rare. Holzapfel, reviewing the literature from 1766 to 1891, found only 21 cases; Biedermann in 20,000 autopsies found only 8 cases. The author describes 2 cases and illustrates them with roentgenograms and diagrammatic drawings. The only way this anomaly can be demonstrated during life is by roentgen examination. The signs which reveal it are: (1) changes in the cardiovascular shadow, the aortic arch being present on the right side and absent on the left; (2) esophageal signs. In the author's cases the esophagus was displaced to the left and an imprint on the esophagus was produced by the median border of the arch, similar to that normally produced on the left border of the esophagus by the normal arch. There was also an imprint on the posterior surface of the esophagus, pushing it forward and constricting the lumen. There were other curved imprints on the esophagus at the level of the bifurcation of the trachea coming from

the front and to the left. (3) The tracheal signs consisted of a displacement to the left, of a lesser degree than that of the esophagus, a displacement forward of a degree proportionate to that of the esophagus and a slight reduction in size. There are other variations in the image depending on the point of origin of the large vessels and the course of the aorta. The details of a number of these images are discussed.

This displacement of the arch of the aorta produces various symptoms, dysphagic, respiratory and cardiovascular. The dysphagia may be due to sclerosis of the aorta or, as the author thinks more probable, to atony of the esophagus.

In order to detect dextroposition of the aorta a thorough examination of the mediastinum and the cardiovascular bundle must be made with accurate roentgenoscopy in various positions and roentgenograms for recording the details that seem significant, also teleroentgenograms in various projections with rays of various penetrations, and the administration of barium paste to control the relations of the esophagus to the aorta.—*Audrey G. Morgan.*

Solis-Cohen, Leon, and Steinbach, Meyer. Sporadic congenital goiter causing death of an infant. *Am. J. Dis. Child.*, Nov., 1939, *58*, 1067–1071.

Solis-Cohen and Steinbach report a case of sporadic congenital goiter causing death of an infant, forty-eight hours after delivery, apparently of pressure asphyxia. Although thyroid enlargement in the newborn is not uncommon in certain districts where goiter is endemic, a perusal of the literature revealed surprisingly few instances of sporadic congenital goiter. The associated syphilis in the mother and the positive Wassermann reaction of the cord blood, together with the anomalous extra digits, present in their patient, they regarded as coincidental phenomena unrelated to the thyroid enlargement. The thyroid found at autopsy was one of the largest on record. The roentgenogram (postmortem) showed a large, evenly outlined mass in the region of the thyroid, protruding anteriorly and laterally. The supracardiac shadow was widened, apparently due to enlargement of the thymus, which was found at autopsy to weigh 10 gm. and was enlarged covering the heart anteriorly and laterally.—*R. S. Bromer.*

ABDOMEN

Bignami, Giuseppe. L'ulcera duodenale nell-'eta giovanile. (Duodenal ulcer in children.) *Radiol. med.*, May, 1939, *26*, 394–409.

Since the development of improved roentgen technique it has been found that duodenal ulcer is much more frequent in children under fifteen years of age than was formerly supposed. Statistics from various authors are published, showing that from less than 1 to 3.5 per cent of their cases of duodenal ulcer were in children.

The author treated 186 cases of duodenal ulcer in the course of twenty months and found that 10 of them, or 5 per cent, were in children from nine to fifteen years of age. He thinks that even this figure is probably lower then the true one, for often roentgenologists, because of the supposed rarity of duodenal ulcer in children, do not make a careful examination for that disease. Moreover the indirect stomach symptoms of duodenal ulcer, such as hypertonia, hypermotility and hypersecretion, are not found in children. If systematic examinations of large groups were made in schools, orphans homes, etc., the author is sure that more of these ulcers would be found.

His 10 cases are described and illustrated with roentgenograms and an extensive bibliography of the subject is given.

There is no definite evidence of constitutional factors in the causation of these ulcers. In most of the author's cases the disease began at from ten to twelve years of age; in the one patient who was only nine years of age the symptoms began at the age of eight. In 2 of the cases there was a history of duodenal ulcer in the father and in another the father had been a stomach patient for years. The symptoms are very much like those in adults except for vomiting, which was seen in only a few of these cases, and hemorrhage and perforation which were not seen in any of them. The roentgen sign of niche was seen in all the cases. The irritative factors, such as alcohol and nicotine, often seen in adults were not present in these cases. Gastroduodenal stasis was probably a causative factor.—*Audrey G. Morgan.*

Mucchi, Ludovico, and Martinet, René. L'ulcera dell'estremo distale della I porzione del duodeno e l'ulcera duodenale extrabulbare. (Ulcer of the distal end of the first portion of the duodenum and extrabulbar

duodenal ulcer.) *Radiol. med.*, April, 1939, *26*, 289–305.

Since the development of improved roentgen technique it has been found that ulcers of the duodenum are much more frequent than those of the stomach. Among 545 cases of ulcer seen at the Royal University of Milan from 1933 to 1937, 398, or 74.7 per cent, were in the duodenum; in 23 cases, or 4.2 per cent, there were ulcers in both stomach and duodenum and in 124, or 21.1 per cent, the ulcers were in the stomach.

The authors made a careful surgical and roentgen study of these 398 duodenal ulcers. There has been a disagreement in the surgical and roentgen findings with regard to the localization of duodenal ulcers. They have frequently been diagnosed as bulbar on roentgen examination and found on operation to be extrabulbar. The authors analyze these findings. The bulb of the duodenum is defined anatomically as that part extending to the upper flexure. Many of the ulcers diagnosed roentgenologically as bulbar were in the terminal part of this tract. Surgically they showed the characteristics of extrabulbar ulcers and were so described by the surgeons. It is true that these ulcers which are anatomically bulbar are surgically to be classified as extrabulbar, for like the true extrabulbar ulcers they are not operable.—*Audrey G. Morgan.*

Bignami, Giuseppe. Quadri radiologici da invaginazione gastro-gastro-duodenale e duodeno-duodenale. (Roentgen images of gastro-gastro-duodenal and duodeno-duodenal invagination.) *Arch. di radiol.*, May-June, 1939, *15*, 255–267.

The author has previously discussed the ordinary forms of intestinal invagination. In this article he describes 2 cases, one of gastro-gastro-duodenal invagination and one of duodeno-duodenal invagination. The first patient was a woman of sixty-nine who for about a year had suffered from loss of appetite, pain in the stomach, particularly after meals, and progressive loss of weight and pallor. In May, 1938, a roentgen examination showed a neoplastic infiltration of the antral region of the stomach. On January 24, 1939, she came for examination because her general condition had grown worse and vomiting had begun. Her blood examination showed 1,460,000 red cells and 25 per cent hemoglobin. Wassermann and Sachs-Georgi reactions negative. Roentgen examination showed that the neoplastic infiltration had resulted in invagination of the proximal part of the stomach into the distal part and of both into the duodenum.

The second case was in a man of twenty-six who about two years ago began to have intense pulling pains in the epigastric region radiating all over the abdomen. Appetite was good. The pain began two or three hours after meals and the patient vomited his food. The vomitus was acid but did not contain blood. The physician who was called diagnosed ulcer and the patient was sent for operation. Roentgen examination showed what was interpreted as retrograde duodeno-duodenal invagination. Operation confirmed the diagnosis. Sclerosis and adhesions around the duodenum had evidently caused the invagination.—*Audrey G. Morgan.*

Medinger, Frederick G. Malignant tumors of the small intestine. *Surg., Gynec. & Obst.*, Sept., 1939, *69*, 299–305.

Of 22 cases of malignant small intestinal tumors, 3 were in the duodenum, 12 in the jejunum and 17 in the ileum. There were 16 carcinomas and 6 sarcomas. When considering this series together with those the author collected, 134 in all, the frequency in the duodenum and ileum is greater than in the jejunum. Carcinomas are more frequently in the upper small intestine and sarcomas in the ileum.

The clinical picture is variable. Biliary obstruction is important in the duodenum and the obstructive feature in the bowel important lower down. Gross bleeding or occult blood is a frequent but not infallible finding. Special roentgenologic study of the small intestine is the best positive means of diagnosis but is not infallible by itself. There was an operative mortality of 30 per cent in the author's series of radical resections. Of the total 19 patients treated by surgery there were 9 deaths. This makes an operative mortality of all surgery of 47 per cent. Eighteen of the 22 patients are known dead, 3 patients are living and well, one eleven years, one three years, and one less than a year. One was lost in follow-up.—*P. C. Swenson.*

Valenti, Alessandro. Echinococco calcificato della coda del pancreas. (Calcified echinococcus of the tail of the pancreas.) *Radiol. med.*, May, 1939, *26*, 436–437.

A woman of fifty-two had suffered for a long

time from vague disturbance with a feeling of weight in the epigastric region; during the past year the symptoms had become worse and had become localized beneath the left costal arch. For the past two years she had had attacks of urticaria. She had never been in contact with dogs. She was in good general health. Below the left costal arch palpation showed a round hard tumor the size of a small orange, with characteristics resembling those of a tumor of the stomach. Roentgen examination of the left upper quadrant showed a round shadow with a calcified outline which was smooth and regular. This shadow was continuous with the lesser curvature of the stomach from which it could not be separated by manipulation.

Median supraumbilical laporatomy showed a cyst with a rather large base implanted on the tail of the pancreas. Resection was rather difficult as the gland tissue bled copiously. The tumor was completely removed and recovery was uneventful. The cyst was round, the size of a mandarin with a thin calcified shell resembling an egg shell. It had a scanty turbid liquid content with vesicles of various sizes scattered through it. Microscopic examination showed many characteristic echinococcus hooks scattered in the vesicles.

This is the 52nd case of this kind reported in the world literature. Thirteen of these cases are in the Italian literature—11 of them operated on and 2 autopsy findings. Very few of the cases were examined roentgenologically and none of the others had such a characteristic roentgen picture as this one.—*Audrey G. Morgan.*

Bignami, Giuseppe, and Secomandi, Giov. Maria. Parassiti epatici e splenici (Pentastomi in particulare) al controllo radiologico ed anatomo-istologico. (Roentgen and anatomo-histological examination of parasites of the liver and spleen (Pentastoma in particular).) *Arch. di radiol.*, May–June, 1939, *15*, 227–254.

The author discusses the anatomical and roentgen picture of various parasites seen in an encysted form in the liver and spleen. Distoma, echinococcus, *Tenia solium* and *Ascaris lumbricoides* are discussed briefly and then a detailed description with roentgenograms given of 2 cases of pentastoma cysts of the liver. Both were in autopsy specimens. There were many small nodules of a grayish-yellow color in the liver. Many of these small nodules were seen—26 in the first case—but only a few of them were visible on roentgen examination. They were round or slightly oval, 2 to 3 or even 4 mm. in diameter. In the specimens not yet completely calcified a typical dentation of the membrane of the parasite was seen. This is the most characteristic feature of pentastoma cysts. When calcification is far advanced only small round spots can be seen which it is hard to differentiate from other structures. Two cases of phleboliths of the spleen are described and illustrated to show the difficulties in differential diagnosis. The roentgen picture of encysted pentastoma differs depending on the stage of development of the larva, the stage of disintegration of the dead larva, the intensity of its infiltration with calcium salts, the intensity of the capsular reaction in proportion to the duration of the infestation with parasites and the number of larvae contained in each nodule.—*Audrey G. Morgan.*

Barbieri, Arrigo. L'indagine radiologica nell-'ascaridiasi.(Roentgen examination in ascaridiasis.) *Radiol. med.*, June, 1939, *26*, 475–506.

The general appearance of ascarids in roentgen examination has been discussed in a previous article. In this article the author takes up the roentgen examination of the different parts of the digestive tract for ascarids. The first part of the digestive tract in which the parasites are found is the stomach and here they are comparatively rare. By irritation of the gastric mucosa they cause an antiperistaltic movement resulting in vomiting. This irritation and possibly also the discharge of toxic products from the parasites causes the pain seen in ascaridiasis of the stomach. This frequently leads to a mistaken diagnosis of ulcer. Roentgen demonstration of the parasites makes differentiation possible. The movement of the parasites is more active in the stomach than in other parts of the intestinal tract.

Ascarids are not frequent in the duodenum yet they are found here more frequently than in the stomach. Specimens have been seen lying partly in the stomach and partly in the duodenum. The symptomatology is that of duodenal ulcer. One case is described in a child six years of age in which the symptomatology was that of cholecystitis with violent pain in the right hypochondrium with vomiting and fever. Examination showed the gallbladder normal and the symptoms seemed to be caused by spasm of the sphincter of the common duct caused by irritation of the duodenal mucosa by the ascarids demonstrated in the duodenum. In some cases

described in the literature there have been no symptoms except atony of the bulb of the duodenum. That the symptomatology was caused in these cases by the ascarids was proved by the fact that the symptoms disappeared after the administration of an anthelmintic.

Segmental dilatation of the intestine is a characteristic sign of ascaridiasis in the small intestine. Ascarids are found more frequently in the small intestine than in other parts of the digestive tract and probably more frequently in the terminal part of the jejunum than elsewhere. Ascarids in the small intestine cause spasticity and hyperkinesis in addition to segmental dilatation. Certain forms of mesenteritis accompanied by the presence of ascarids in the intestine are believed not to be caused by the parasites.

The relationship between ascarids and appendicitis is also discussed. The author brings forward the roentgen evidence and concludes that the parasites simply produce a local irritation but not a true appendicitis. This irritation may be caused by groups of ascarids in the cecum or near the ileocolic sphincter without their actual presence in the appendix.

In the large intestine dead ascarids are more frequent than living ones. The most frequent symptom in these cases is occlusion. Examination without a contrast medium is particularly valuable in demonstrating these occlusions from ascarids. While perforation of the intestine sometimes occurs in cases of ascaridiasis the author does not believe that it has been proved that the parasites cause the perforation.

Roentgenograms are given of unusual cases of ascaridiasis in the digestive tract.—*Audrey G. Morgan.*

Benassi, Enrico. Occlusione duodenale da voluminoso calcolo biliare. (Occlusion of the duodenum by a large bile calculus.) *Radiol. med.*, June, 1939, *26*, 562–563.

A woman of seventy after a preliminary period of three or four months of general malaise, loss of appetite and weight, was taken suddenly with vomiting of food followed by uncontrollable vomiting of a black liquid with hiccough and violent epigastric pain. She was sent to the hospital immediately for roentgen examination with a probable diagnosis of stenosis of the pylorus from tumor.

Examination showed no signs of neoplasm of the stomach but showed that the first portion of the duodenum was displaced backward and enormously dilated and evidently contained a large foreign body, as only a small amount of contrast medium entered it, arranged in concentric stripes along the wall. The distended duodenum had compressed the pylorus.

Surgical operation showed the gallbladder adherent to the duodenum; the first portion of the duodenum, greatly dilated, was filled with a large calculus. The bulb of the duodenum communicated with the gallbladder by an opening which admitted a finger. The calculus was the shape of a pear and about 7×5 cm. in size.

The case is interesting because of the rarity of migration of such a large calculus into the duodenum, and it shows how necessary a preliminary direct examination of the abdomen is in cases of acute abdominal symptoms.—*Audrey G. Morgan.*

GENITOURINARY SYSTEM

Pulvertaft, R. Guy. Nephrolithiasis occurring in recumbency. *J. Bone & Joint Surg.*, July, 1939, *21*, 559–575.

Pulvertaft had the opportunity of studying 60 cases of nephrolithiasis occurring in recumbency. He thinks undoubtedly that prolonged recumbency may lead to the formation of renal calculi. This is chiefly due to the combination of defective renal drainage and skeletal decalcification. The composition of the calculi is usually calcium phosphate. Hematuria and abdominal pain may follow alteration in posture and may lead to the discovery of the stone, although in some cases the stone may be unsuspected until revealed by the roentgenogram. Patients who need to be recumbent for long periods should undergo postural treatment and have routine roentgenographic examination of the renal tract. Many of these calculi occurring in recumbency disappear when the erect posture is resumed, but a large porportion remain and may require surgical removal. The occurrence of stone may be a fatal complication.—*R. S. Bromer.*

Orsenigo, Serafino. L. Calcificazione della vaginale del testicolo. (Calcification of the vaginal sheath of the testicle.) *Radiol. med.*, June, 1939, *26*, 561–562.

Roentgen examination was made of a man eighty-one years of age because of suspected fracture of the head of the right femur. Calcification was shown in the region of the right testicle, forming a cap which covered the outer and upper part of the testicle. This was evidently

due to calcification of the vaginal sheath of the testicle. There was no evidence of specificity and the man gave a history of an injury of the testicle at the age of ten which had kept him in bed for several days on account of pain. There were no sequels. The man was in good health and had had 12 normal children. Evidently the calcification had resulted from hemorrhagic periorchitis caused by the trauma.—*Audrey G. Morgan.*

SKELETAL SYSTEM

Sontag, L. W., Snell, Dorothy, and Anderson, Margaret. Rate of appearance of ossification centers from birth to the age of five years. *Am. J. Dis. Child.*, Nov., 1939, *58*, 949–956.

Numerous methods have been proposed for appraising the skeletal changes in child development. The various methods take into consideration to a greater or lesser degree bone growth as well as differentiation, but there is little agreement as to the relative significance or the degree to which the two factors conform. The bones of the human body undergo changes in shape and function as well as changes in size.

The authors present a scale for rating progressive skeletal development of boys and girls from birth to the age of five years, based on data obtained in a study of longitudinal growth. All joints of the left upper and lower extremities are given equal rating with the hand in appraising the skeletal growth. The advantages of this scale, they claim, are that no great skill is required to count the number of centers of ossification and that the results are rapidly and objectively achieved. It is a flexible and convenient method of evaluating skeletal age for correlation with other factors of growth, nutrition and environment. Their method is applicable only to the early age levels, since it is during this period that most of the centers appear. It is the only method they have found in which the limit of error of each estimation is small enough to enable them to determine and express numerically the skeletal progress of an individual child at successive age levels. It makes no pretense, however, of measuring the progress of maturation of centers once they have appeared. —*R. S. Bromer.*

Kazanjian, V. H. Congenital absence of the ramus of the mandible. *J. Bone & Joint Surg.*, July, 1939, *21*, 761–772.

Kazanjian reports 5 cases of unilateral absence of the mandible, a rare deformity. This anomaly is a clear-cut defect, which has been described under a variety of titles, thus making it difficult to discover in the literature. It is often associated with microtia and at times with unilateral fissure of the mouth.

Embryologically, this defect is thought to be caused by improper development of the various elements of the first branchial arch and cleft. Other facial and cranial bone anomalies, however, are present rather often, especially in the temporal bone. The question, Kazanjian says, may be raised whether these anomalies are not secondary to the absence of the mandibular segment, which thus deprive the surrounding tissues of a normal growth stimulus. The 5 reported cases were collected over a period of eight years. The treatment in general was conservative, except in the case of the soft-tissue defects. The repair of mouth fissures and the building up of the ear when absent was not delayed. He considers the treatment of the mandibular defect is best postponed until the permanent teeth have erupted to permit the use of proper splinting and for other considerations outlined in detail. Orthodontic measures should be instituted early.—*R. S. Bromer.*

Dobelle, Martin. An unusual location of an osteochondroma. *J. Bone & Joint Surg.*, July, 1939, *21*, 781–784.

Dobelle reports a case of osteochondroma located on the costal surface of the scapula. Located in this area, the lesion may exist without any subjective symptoms and its peculiar location may mask its presence on physical examination. More of these cases may perhaps be found, he thinks, if the possibility of their existence is borne in mind. In his case pain was never experienced during scapular movements. The objective finding reported by Brown—"The scapula at times in sliding over the ribs would catch and jump from one rib to another"—was closely paralleled in Dobelle's case. He quotes Christensen's analysis of 1,000 cases of bone tumors which showed that 15 were confined to the scapula, of which 14 were malignant and only one benign. Such an overwhelming percentage of malignancy warrants careful clinical and roentgenological study of scapular tumors before a diagnosis of a benign lesion is made.—*R. S. Bromer.*

De Santo, Dominic A., and Wilson, Philip D. Xanthomatous tumors of joints. *J. Bone & Joint Surg.*, July, 1939, *21*, 531–558.

Xanthomata of the synovial membrane of the joints, the authors believe, are probably more common than has hitherto been supposed, as is exemplified by their group of 9 cases collected over a brief period of time. Their paper is based upon an analysis of 41 cases of which 32 are quoted from the literature and 9 are from their own series.

The preoperative diagnosis of joint xanthoma seems never to have been made. Obscure intermittent swelling of the knee joint, associated with pain and free fluid, occasional locking, and a movable tumor usually medial to the patella, will frequently be found to be caused by xanthoma. Aspiration, with recovery of an orange, brown, or sanguineous, thick, oily fluid is very significant, and the demonstration of cholesterol also substantiates the diagnosis, although a normal figure by no means excludes it. The tumors occur predominantly in the knee joint. Other locations were the ankle joint and the joint between the navicular and the second cuneiform bones.

Roentgenographic examination was reported negative in many cases. In other cases it showed the presence of considerable exudate within the joint, distention of the joint capsule, or swelling of the soft parts. Occasionally the shadow of a soft tissue tumor was revealed. When the joint symptoms had caused long-standing interference with function, moderate decalcification of bone structure was found. When there had been erosion of the bone from pressure of the tumor, this also was demonstrated.

Xanthomata originate in chronic hemorrhagic villous arthritis. In their histological picture the stroma cell, which is found, is related to the reticulo-endothelial system. It is derived from the surface synovial-membrane mesothelium, which has reticulo-endothelial properties, and gives rise to: (*a*) the foam cell, (*b*) the giant cell, and (*c*) the pigmented cells found in xanthomatous tumors.

The joint xanthomata are related to some fundamental disturbance of lipoid metabolism. The blood cholesterol is frequently elevated. Cholesterol formation probably takes place locally as a result of interstitial hemorrhage and is a decomposition product of hemoglobin. Its failure to be found universally when interstitial hemorrhage occurs is partially explained by the systemic disturbance of lipoid metabolism which usually exists.

De Santo and Wilson found no instance of a benign giant cell xanthoma undergoing malignant transformation. They state the joint xanthomas can be cured by radical excision. In the case of solitary tumors, local excision is sufficient, but in the case of multiple or diffuse involvement, a subtotal or total synovectomy is usually necessary.—*R. S. Bromer.*

Bradford, F. Keith, and Spurling, R. Glen. Intraspinal causes of low back and sciatic pain. *Surg., Gynec. & Obst.*, Oct., 1939, *69*, 446–459.

Sixty consecutive cases are reviewed in which a lumbar laminectomy was done for the relief of low back and sciatic pain. There were 35 cases of herniated nucleus pulposus, 13 of hypertrophy of the ligamentum flavum and 3 of true neoplasms and 9 negative explorations. The symptoms are reviewed with pain as a disabling factor in 59 of the cases. The diagnosis of the four groups is discussed, both by the symptoms and the use of lipiodol intraspinally. The surgical treatment and pathology are also discussed and the results of surgical intervention. The high frequency of occurrence of nucleus pulposus prolapse and ligamentum flavum lesions is emphasized. The correlation of roentgen and clinical findings must be carefully done in order to insure successful selection of cases for operation. Lipiodol in the hands of the authors has been a safe procedure, 2 cc. being adequate for intraspinal injection. The authors conclude that lesions low in the spinal cord are the commonest single cause of chronic low back and sciatic pain in the group of patients in whom no bone disease is demonstrated in the lower spine or pelvis.—*P. C. Swenson.*

Bishop, W. A., Jr. Vertebral lesions in undulant fever. *J. Bone & Joint Surg.*, July, 1939, *21*, 665–673.

Bishop's case is the fifty-seventh reported of spondylitis complicating undulant fever. *Brucella suis* was isolated from the blood stream after the development of the local lesion, which occurred over a year after the initial infection. The lesion in the lumbar spine was treated by surgical fusion, and the cervical lesions by support, with improvement after seven months.

The clinical appearance is the result of the hematogenous localization of bacteria, ordi-

narily in the osseous marrow, but exceptionally in the disc in young individuals. A study of the roentgenograms of the reported cases and his own showed a variability of the site and extent of spinal lesions. In some, only an angle of the vertebral body, occasionally both or all of the surfaces were invaded. The lesion may be confined to the disc, but seldom results in narrowing of the intervertebral space by more than one-half. In the latter cases, there is usually involvement of a part of the adjacent vertebral surface. The contour of the body often remains normal and practically always appears sclerotic or irregular. Very frequently, the initial lesion in the body is masked by concomitant periosteal reaction as evidenced by spur formation. These frequently appear only at the anterior margins of the bodies, but occasionally they are also seen in the anteroposterior view to follow the contour of the disc. A rare occurrence is involvement of the intervertebral articulations.

The case studied in the more advanced stage of the process revealed a constant and characteristic roentgenographic picture. All showed a reactive change, increased calcifications of the bodies, circumscribed or diffuse, with proliferation of bone spurs across the interspace. Sometimes in the more severe cases, there was some deformity of the body or involvement of the articular facets. Bony fusion of the bridges between the adjacent bodies was a common finding.

The complication originates usually in the convalescent stage of undulant fever, but may make its appearance at any time. It is accompanied by a febrile reaction, and is characterized by the acuteness of the symptoms and a benign clinical course.—*R. S. Bromer.*

McCarroll, H. R., and Crego, C. H., Jr. Primary anterior congenital dislocation of the hip. *J. Bone & Joint Surg.*, July, 1939, *21*, 648–664.

The authors state that three distinct types of congenital dislocation of the hip joint can be clearly recognized and differentiated. The first type is the classic posterior dislocation. The second type consists merely of an upward subluxation of the femoral head as the result of an inadequate superior rim of the acetabulum. The third type is that which exists in a true anterior position with the femoral head pointing directly forward, resting just behind and below the anterior superior spine.

They report 10 cases of primary anterior congenital dislocation of the hip and each of the patients presented the following cardinal characteristics:

1. Absence of lumbar lordosis.
2. There is less shortening in such patients than is usually seen in the other two types of congenital dislocation of the hip.
3. The buttock on the affected side is flatter than normal.
4. A bulge is present anteriorly just below the anterior superior spine, marking the position of the femoral head, which can be often outlined visually.
5. The femoral head can be felt pointing directly forward just below the anterior superior spine.
6. Lateral roentgenograms of the pelvis reveal a true anterior position.
7. All anterior dislocations have recurred following closed reduction even when preceded by preliminary skeletal traction.

Their treatment consists of preliminary skeletal traction followed by attempted closed reduction and if this is successful, the torsion is corrected by supracondylar osteotomy. In their experience, however, anterior dislocations have invariably recurred after weight-bearing was instituted. They again resort to preliminary skeletal traction followed by open operation in which an attempt is made to reduce the femoral head, although this is usually impossible. In either instance, a wide shelf of bone is placed extracapsularly above the femoral head along the superior rim of the acetabulum, extending forward to include the anterior superior spine. In this way adequate stability is assured even though reduction is not possible or does not persist. Results in their cases have been satisfactory up to the present time, although no case has been followed one year after the removal of the final plaster.—*R. S. Bromer.*

Phemister, Dallas B. The pathology of ununited fractures of the neck of the femur with special reference to the head. *J. Bone & Joint Surg.*, July, 1939, *21*, 681–693.

Ununited fractures of the neck of the femur, Phemister states, are distinctive for their relative frequency and resistance to operative treatment. These in turn are dependent in large degree on structural peculiarities of the hip, fractures of which result in pathological change that is not ordinarily seen in fractures of other

parts of the skeleton. These peculiarities are: (1) the approximately 125 degree angle of the neck to the shaft, resulting in marked shearing and erosion of the neck fragments; (2) the absence of a cambium layer in the fibrous covering of the neck with no peripheral callus formation in the healing process; and (3) the variable arrangement of the blood supply of the head, which, in case it is derived from the neck vessels, may be cut off by the fracture with resultant necrosis of the head fragment.

Phemister discusses the pathology of ununited fractures of the neck of the femur with special reference to the head in terms of three questions. The first question, namely, "By what signs in the roentgenogram do you determine whether the head is viable or alive?" is of great interest to the roentgenologist. A viable head with non-union may usually be determined in roentgenograms by the presence of disuse atrophy, giving even reduction in density, about equal in all portions of the head, upper end of the shaft, and the adjacent pelvis. These density changes are usually present by the time that the evidences of non-union can be made out, and they usually last as long as the fracture remains ununited. In case of long-standing non-union, the articular surface of the head retains its normal contour, and the cartilage space and articular cortices remain intact. If operation is performed resulting in bony union, and if function is restored, the bone again increases in density. Union following operation is more common than in the case of a necrotic head. Subsequent collapse of its weight-bearing portion does not take place and the functional result is usually a good one.

If there is destruction of the blood supply with necrosis of the head, collapse follows after operation with marked irregularity of its joint surface. If non-union is present there is atrophy of disuse of the living bone of the shaft and pelvis while the dead bone in the head retains its original density. Consequently after two or three months, the head may be seen to cast a denser shadow in roentgenograms than the surrounding living bone. However, invasion of the marrow spaces of the dead head soon begins by blood vessels and fibrous tissue through the round ligament, untorn portions of capsule, and later through adhesions. As this invasion proceeds, it is followed by creeping substitution of the dead bone and fibrous marrow by a less dense living bone and hemopoietic marrow. The lower mesial portions of the head are usually invaded and transformed first. The process extends upward and outward from the fovea and lower portions at an extremely variable rate. Usually in the course of a few months the transformed lower and mesial portions of the head may be distinguished in roentgenograms by their marked reduction in density in contrast to the rest of the head, which has preserved its original density.

Necrotic heads that have been completely replaced by new bone may be extremely porous with irregular articular surfaces and are usually bound to the acetabulum by extensive adhesions. They may be recognized in roentgenograms by their porous nature and blurred, uneven shadows of articular cortices. In some cases the dead head is very slowly invaded by fibrous tissue, and there is little replacement of the invading dead bone by new bone and hemopoietic marrow. It is very difficult to understand why replacement takes place rapidly in some cases and very slowly in others.

The second question discussed by Phemister is: "Do you consider it possible to restore sufficient blood supply to a devitalized head to warrant saving it?" The only way a surgeon may help to restore circulation to a devitalized head is by an operation which results in bony union. He cites a case to show that bony union and a good result may follow operation for non-union when necrosis of the head is present.

The third question which was put to the author, "In the light of the studies of the pathology of the femora which you have made, what types of operation do you believe are indicated for this condition?" is discussed in detail. Operative measures which have been employed for early and late cases are described.—*R. S. Bromer.*

Milch, Henry. Internal-rotation-brace treatment of epiphyseal coxa anteverta (early epiphyseolysis). *J. Bone & Joint Surg.*, July, 1939, *21*, 752–760.

Epiphyseal coxa anteverta is the term which has been suggested to define the first stages of the condition which has been called separation of the upper femoral epiphysis or epiphyseolysis. The designation "epiphyseal coxa vara" Milch states is misleading and should be discarded because varus is a late and not a primary manifestation of the affection. Clinically, the first signs of onset of the disease are pain, limping, and then interference with function in the hip of adolescent individuals. Roentgenographically,

the pathognomonic sign is a so-called "widening of the epiphyseal line." The prognosis becomes materially worse if treatment is undertaken late in the course of the disease; therefore, the necessity for early diagnosis and immediate emergency treatment, as for fracture, is stressed.

Milch suggests the internal-rotation-brace treatment of epiphyseal coxa anteverta because it appears to have given satisfactory results. The brace affords a ready, efficient and inexpensive method of preventing a further progress of the lesion and of maintaining the position of the parts until complete healing has occurred. In one or two cases he gained the impression that the brace acted as a correcting force, tending to reduce the degree of anteversion present at the beginning of the treatment. —*R. S. Bromer.*

Barber, C. Glenn. Congenital bowing and pseudarthrosis of the lower leg; manifestations of von Recklinghausen's neurofibromatosis. *Surg., Gynec. & Obst.*, Nov., 1939, *69*, 618–626.

The author presents 5 cases demonstrative of the association of pseudarthrosis and congenital bowing of the lower legs with von Recklinghausen's neurofibromatosis. Heretofore, this association has not been reported in the literature of this country or Great Britain. Added to the 9 typical and the one atypical cases reported by Ducroquet this makes a total of 15 cases submitted for publication. Of this number 13 reveal a definite and identical etiology in which the aforementioned orthopedic variations are manifestations of von Recklinghausen's neurofibromatosis.—*P. C. Swenson.*

Kulowski, J. The management of hematogenous pelvic osteomyelitis. *Surg., Gynec. & Obst.*, Sept., 1939, *69*, 312–326.

The present day concepts of the management of hematogenous osteomyelitis have developed from a better knowledge and interpretation of the clinical life history of this disease in the long bones, but particularly in the pelvic girdle where it presents a unique problem. Divergent opinions of conservative and radical treatment have dovetailed under the present ideas of operative management. Operation is contraindicated until definite suppuration has occurred, and the exact determination of this point is of primary importance, thus the surgeons gravest responsibility. To operate on mere suspicion of a lesion is impractical and dangerous. The presence of suppuration is the sole indication for initial operation in the early stages of the disease. The local and systemic benefit derived from a well timed simple incision and drainage is indisputable, but this is not always followed by a dramatic recession of symptoms. The disease may continue as a severe local or general infection until the defensive mechanisms of the body begin to establish controlling influences. Radical intervention belongs to the residual phases of the disease and is determined by the qualitative and quantitative state of the local lesion on its own merits.

Treatment is dependent upon the early recognition of the disease and a knowledge of the state of development of the local lesion and its relation to the systemic factors.

A perspective of hematogenous osteomyelitis is presented from the viewpoint of its pathogenetic development on the basis of which a clinical grouping of cases is possible for a more intelligent therapeutic management. Examples of this clinical grouping are given.

The author considers adequate roentgenograms indispensable for differential diagnosis and careful operative planning.—*P. C. Swenson.*

Trivelli, Luciano. Contributo allo studio del l'osteoartropatia ipertrofizzante pneumica. (Study of hypertrophying pneumonic osteoarthropathies.) *Radiol. med.*, April, 1939, *26*, 305–317.

This name is applied to a disease in which there is thickening of the bones, especially their distal ends and near the joints due to new formation of bone from the periosteum. In 1890 Pierre Marie described 8 cases with a clinical syndrome in which there were changes in the bones of the hands and feet with the characteristic drumstick fingers because of an osteophytic process in the bones. This was found not to be a primary disease but a syndrome secondary to other diseases and, as Marie thought that the primary disease was always in the lungs, he added the adjective pneumonic to the name.

It has since been found, however, that the primary disease is not always a disease of the lungs. The author described 4 cases and illustrates them with roentgenograms showing the characteristic enlargement of the distal ends of the bones. In one of these cases the primary disease was a polycystic lung, in 2 pleural emphysema but in the other it was a tuberculosis of the intestines. The enlargement of the bones began

so gradually in this case that the patient himself did not notice it for a considerable time. This case differs from most cases of Marie's disease not only in the fact that it followed tuberculosis of the intestine, which is extremely rare, but in that there was no pain in the beginning of the joint involvement. Nearly always there is acute pain.

The author thinks the name adopted by Marie justified because the majority of the cases follow lung disease.—*Audrey G. Morgan.*

Picchio, Carlo. Condromatosi articolare calcificata. (Calcified joint chondromatosis.) *Radiol. med.*, May, 1939, *26*, 437–439.

A housewife forty-five years of age had for several years noticed multiple small tumors on her right wrist; they were painless and developed slowly. Roentgen examination showed subcutaneous neoformations of wooden hardness, some of them isolated from each other and some of them fused into larger masses. They lay along both sides of the carpal bones but the bones themselves and the joint spaces were free. They were mulberry-shaped and made up of fine granules. Examination of the other joints did not show any changes. Histological examination of one of the nodules showed "calcified chondroma.

This case is clinically and roentgenologically characteristic of calcified joint chondromatosis. These cases are rather rare in the wrist; about 40 per cent of the cases are in the knee joint, 25 per cent in the elbow, 10 per cent in the hip and the rest distributed among the other joints. They are to be classified as free bodies in the joints rather than as true tumors.—*Audrey G. Morgan.*

Bignami, Giuseppe, and Runco, Antonio. Iconografia radiologica di anomalie di sviluppo degli arti. (Roentgen iconography of anomalies of development of the lower limbs.) *Arch. di radiol.*, May–June, 1939, *15*, 191–214.

The authors give detailed descriptions of anomalies of development of the limbs in 10 cases, 3 of them being fetal monsters with fusion of the lower limbs. In the other 7 cases in adults there were various anomalies of the bones of the upper and lower limbs, illustrated by roentgenograms. The only classification he gives of these anomalies are into those caused by defective formation of bone and those due to fusion. He suggests, however, that data of great scientific interest can be obtained by a further careful study of the various forms of congenital anomalies, their classification and an attempt at determining their causes.—*Audrey G. Morgan.*

Anspach, William E., and Huepel, Robert C. Familial cleidocranial dysostosis (cleidal dysostosis). *Am. J. Dis. Child.*, Oct., 1939, *58*, 786–798.

Anspach and Huepel report the occurrence of familial cleidocranial dysostosis in a father and 3 daughters of a family in which there were 9 members. All 4 were short of stature and all had prominent frontal eminences and parietal bosses, median furrows of the skull, markedly defective dentition of a special type and abbreviated distal phalanges, especially of the thumbs and great toes. The children showed wide sutures and epiphyseal lines with marked delay in time of closure and mild rickets-like changes in the bones.

The father stated that he had retained his deciduous teeth until the age of thirty years and the 3 daughters, aged five, eleven, and fourteen years, when first examined also showed retention of deciduous teeth. The absence of the clavicles, the presence of the sagittal furrows and the epiphyseal changes are all illustrated by roentgenograms. The literature is carefully reviewed. The family is presented by the authors as an example of hereditary defects the cause of which is a defective growth mechanism starting early in embryonic life and asserting itself throughout life. They place emphasis on the presence of defective cartilage throughout a large portion of the skeleton. Changes in the ossification of the pelvic bones are demonstrated they believe, for the first time.—*R. S. Bromer.*

Bignami, G., and Runco, A. Miosite ossificante progressiva. (Progressive myositis ossificans.) *Arch. di radiol.*, May–June, 1939, *15*, 125–190.

The first case of this disease was described in 1649 by Guy Patin. The first thorough description of its pathological anatomy was written in 1869 by Münchmeyer who gave it the name of progressive ossifying myositis. Up to the present time about 200 cases have been described in the world literature, 16 of them in Italy. The author gives brief reviews of the Italian cases and then gives a very detailed description of a case of his own.

The patient was a woman born in 1909. She was not seen by the authors until 1925 but she

had been treated elsewhere since she was about four years of age. The first signs of the disease had developed at the age of about two years when a swelling of the trapezius muscles appeared near the vertebral insertions of the muscles. There was moderate pain, spontaneously and on palpation of the swollen masses. Soon hard nodules began to form in these masses, which increased and became confluent until the whole mass was of the consistency of bone. Gradually the process extended to other bones and successive areas became involved. The progress of the disease is shown by photographs and roentgenograms. The patient never showed any changes in the skin over the affected areas or any fever. Her intelligence was approximately normal although she seemed rather childish and did not appreciate her condition. Toward the end of 1927 when the intercostal muscles became involved she had attacks of intense pain. She had intermissions of weeks, months or even years but in spite of this the disease was steadily progressive. The joints became involved and in 1927 there was fixed flexion of the trunk and semiflexion of the legs on the pelvis. The forearms were still movable. There was only slight mobility of the thorax on respiration, limited to the left half. Examinations for syphilis and tuberculosis were negative. There was no family history of deformity. The changes in the various muscles are described in detail.

This disease generally begins very early in life and frequently there are congenital deformities of the bones of the hands and feet as there were in this case. There are three stages of the disease, that of infiltration, that of induration and fibrous retraction and the terminal stage of ossification. The disease generally begins in the muscles of the neck or shoulder and proceeds downward. In the last stage distinct ossification of the muscles can be seen roentgenologically, even with the development of a marrow cavity. The process generally reaches a stationary stage at about the age of twenty-five.

No effective treatment has been found. Surgery generally only increases the process of ossification. Some authors have recently reported, however, that roentgen treatment in the early stages of the disease, when there is only hyperplasia of the cells, sterilizes the germinative tissue and prevents ossification; it also seems to further absorption. Sgalitzer says that with repeated irradiation of the parts already affected with muscle rigidity with small doses over large fields he has had good results in preventing ossification and even decreasing the hardness and rigidity of the muscles and increasing their mobility.—*Audrey G. Morgan.*

BLOOD AND LYMPH SYSTEM

Bignami, Carlo. Dimostrazione radiografica di aneurisma venoso cirsoideo. (Roentgen demonstration of a cirsoid venous aneurysm.) *Radiol. med.*, April, 1939, *26*, 342–344.

A workman, seventeen years of age, fell from the height of the first story and struck on his right arm. It pained him for a few days but there was no sign of hematoma or swelling and no loss of function. Ten years later, a few days before coming for examination, the patient noticed enlargement of the right arm and weakness of the muscles and finally pain, especially at night and on movements of extension.

Examination showed the arm in partial flexion. At the middle third of the arm there was a fusiform swelling about 10 cm. long. The circumference of the arm was 3 cm. greater than that of the left arm. The skin over the swelling was normal. The swelling was soft and elastic, about the size and shape of a hen's egg. There were no adhesions to the skin or underlying tissues. The radial pulse was normal and of the same rate and strength as that on the left. Blood pressure was the same in both arms.

Roentgen examination in the lateral projection showed a mass which seemed to be a part of the triceps muscle and deformed it. The opacity of the mass in the proximal part was about the same as that of the muscle but in the distal part it was irregular and there were small areas of less density. This suggested a vascular lesion. A puncture led to the discharge of bright red blood. The contrast medium was distributed in many small cavities communicating with each other. A small vessel ran upward from the swelling and emptied into the axillary vein. A diagnosis of metatraumatic cirsoid aneurysm was made. The mass was removed after ligation of the afferent vessel and the diagnosis was confirmed.—*Audrey G. Morgan.*

GENERAL

Warren, Shields, and Hoerr, Stanley O. A study of pathologically verified epidermoid carcinoma of the skin. *Surg., Gynec. & Obst.*, Dec., 1939, *69*, 726–737.

The authors present a statistical study purporting to evaluate the factors influencing the

cutaneous malignancy, epidermoid carcinoma. The material is derived from 507 consecutive cases of pathologically verified and graded epidermoid carcinoma of the skin on 486 persons seen at the Collis P. Huntington Memorial Hospital in the twenty-five year period between 1912–1936. Graded histologically, 382, 75 per cent, were Grade 1; 114, 22 per cent, were Grade 2; 11, 3 per cent, were Grade 3. Ninety-five of the lesions, 19 per cent, were known to end fatally. Of prognostic significance, the size of the lesion when first treated influenced the outcome more than any other factor: lesions larger than 5.0 cm. carried an 82 per cent mortality whereas those of 1.0 cm. or less a 7 per cent mortality. The histological degree of malignancy was next in importance, Grade 2 plus Grade 3 lesions presenting a 5 to 20 per cent greater mortality than Grade 1 lesions for any given size larger than 1.0 cm. Other factors influencing a poor prognosis were treatment prior to coming to the hospital and metastases at the time of admission. The study of the therapeutic results of the cases treated prior to January 1, 1933, indicated that radium (the source, radon in surface emanation) was less satisfactory than surgical excision. An analysis of outcome according to succeeding time intervals showed an improvement over the most recent one (1928–1932 inclusive). The authors attribute this to the greater proportion of small lesions seen during this period rather than to any fundamental improvement in therapeutic technique.—*P. C. Swenson.*

Ghormley, Ralph K., and Pollock, George A. Multiple myeloma. *Surg., Gynec. & Obst.*, Nov., 1939, *69*, 648–655.

In an effort to discover any facts that might strengthen the diagnostic approach to this disease, the authors have analyzed the findings in 86 out of 120 cases in which the diagnosis seemed certain. The presentation is simplified by dividing the group of 86 cases into 5 groups according to the diagnostic evidence and outcome. A summary of the interesting features revealed that 63 of the 86 cases were in males and 23 in females. The incidence according to age was fifty-two in men and 49.6 in women, the youngest patient, a boy of four years and the oldest, a man of seventy-five years. The duration of the disease, 26.9 months, approximated the sub-group of proved cases (postmortem and biopsy), 26.8 months. The data concerning the blood chemistry presented many variations from the normal, but according to the authors: "It is doubtful that any can be considered more than a help in making the diagnosis." As a reliable diagnostic aid, a consistent variation was not apparent in the albumin-globulin ratio, calcium, phosphorus, or phosphatase and the determination of basophilia or eosinophilia. Bence-Jones proteinuria was present in only 51 per cent of the entire group of cases, whereas evidence of renal damage was apparent in 61 per cent of the cases. The authors stress this difference as indicative of the fact that the excretion of this protein cannot always be the cause of the renal damage most likely present in all cases before death. Unlike the typical case in a man past middle age complaining of backache who upon examination presents the roentgen and laboratory evidence of the disease, the authors emphasize the atypical case in which all diagnostic evidence is lacking save that which biopsy can offer.

Only 2 of the patients are alive five and eight years respectively after the onset of the disease. They subscribe to the prognostic viewpoint of Meyerding that "The prognosis, therefore, may be said to be uniformly poor, but in some cases, the disease tends to be more or less arrested by the use of roentgen therapy."—*P. C. Swenson.*

Kretschmer, Herman L. Problems in differential diagnosis between urologic and abdominal lesions. *Surg., Gynec. & Obst.*, Nov., 1939, *69*, 671–683.

The author emphasizes the rôle of the urologist in the differential diagnosis of abdominal disease. In a broad sense the diagnostic problems include: (1) the intra-abdominal and retroperitoneal lesions that might be confused with urological lesions; (2) the postoperative complications in the genitourinary tract; (3) complications secondary to pathological processes that might be confused with urological lesions; (4) complications arising in the postoperative phase from lesions hitherto unrecognized. As exemplifying these groups, he discusses and supplements with case reports: lesions of the gastrointestinal tract; the gallbladder; subphrenic abscess following pregnancy; cyst of the pancreas; carcinoma and diverticulitis of the colon; acute pyelitis following operations; lesions of the gynecological region; pathology of the spine including arthritis, vertebral lesions, and prolapse of the nucleus pulposus; hydronephrosis; retroperitoneal tumors; elusive ulcer; and the differentiation between ascites and

chronic urinary retention. The illustrative cases point out that the clinical acumen of the urologist must reach well beyond the anatomy of the urinary tract and associated structures.—*P. C. Swenson.*

ROENTGEN AND RADIUM THERAPY

Reding, R. Über die Allgemeinwirkungen der Strahlen auf den Organismus. (The general effects of irradiation on the organism.) *Strahlentherapie*, 1940, *67*, 136–138.

It is a definitely established fact that the reactions occurring in the body after irradiation influence considerably the therapeutic effect. Even in carcinoma therapy it is no longer assumed that the radiation has an exclusive effect directly upon the carcinoma cells; we know that also the medium in which the cells live undergoes considerable physico-chemical change resulting from the rays, which are not irrelevant. The irradiation reaction on the body juices takes many phases: Immediately after the radiation there is observed a slight transitory acidosis. Two to three days later there occurs an alkalinization wave of a longer duration which in carcinoma patients where the irradiation effect is unfavorable persists and in those with a favorable effect is substituted by a normal reaction.

The radiation influences the glyco-regulatory mechanism. In carcinoma patients there is observed, when the carcinoma leads to a cure, a hyperglycemia similar to that observed following irradiation of normal individuals. If the irradiation is ineffective the deviations from the normal become even greater. Immediately following the irradiation there appears in carcinoma patients, as well as in normal individuals, a glycemia which later disappears.

These changes are not related to the irradiation of the tumor proper or to the absorption of its decomposition products. They appear in healthy as well as in carcinoma patients in a similar manner.

The changes in the mineral metabolism are parallel to those occurring in the pH. Immediately after the irradiation there occurs a hypercalcemia which is replaced by an even more pronounced and even longer lasting hypocalcemia. In normal individuals the cholesterin level of the blood decreases and this occurs also in successfully irradiated carcinoma patients; in unsuccessfully irradiated carcinoma patients the cholesterin level of the blood increases.

The vago-sympathetic system undergoes a change following irradiation in the sense of a vagus stimulation.

Immediately after the irradiation there occur changes in the blood expressed in the form of a leukopenia and a decrease of the polymorphonuclear cells and followed in a few days by a transitory elevation of the leukocyte count. A slight irradiation stimulates the reticulo-endothelial system while irradiation with high doses paralyzes it.

The biologic effect of irradiation must be looked upon as a shock effect. The cause of the shock is apparently due to a type of a toxin originating in the irradiated tissue. On the basis of the data presented above, it may be stated that from the results obtained immediately after the irradiation in the body juices, one can prophesy whether the irradiation will have a favorable or an unfavorable effect. There seems to exist a definite parallelism between the humoral changes occurring following irradiation and the changes demonstrable in the mitosis of the cells of the tumor proper. On the basis of the changes resulting from irradiation, the author believes that irradiation outside of the carcinoma field is indicated in the following: The treatment of general infections, the treatment of endocrine disturbances and in irradiation following operations.—*A. Schwartzman.*

Wendlberger, J. Zur Röntgennahbestrahlung von Hautkrebsen. (Close roentgen irradiation of skin carcinoma.) *Strahlentherapie*, 1940, *67*, 51–60.

Up to a few years ago, the treatment of primary carcinoma of the skin was associated with considerable difficulty. With the introduction by Chaoul of the close roentgen irradiation in the treatment of malignant tumors, conditions have changed considerably. Chaoul and others have shown that principally there exists no difference between the roentgen rays and the gamma rays of radium. The concentrated fractional close irradiation represents basically a procedure which has the same therapeutic effect as the radium. The similarity with radium is achieved predominantly as a result of the finding that the roentgen rays used are of the soft type and the distance of the focus from the skin is at a minimum. By the aid of fractioning it is possible to introduce into a given field a very large dose without any danger of injury. In this manner the tumor cells can be destroyed with

certainty while the neighboring healthy skin and the healthy tissues under the tumor remain unaffected. The prerequisite for the application of the method of irradiation under consideration is a localization of the tumor which is easily accessible; that is, the tumor must be situated superficially. The domain of close irradiation is therefore the malignant tumor forms of the skin.

Also this author had an opportunity to treat 50 cases by this method of concentrated fractionated close irradiation. In each case the carcinoma was verified histologically. Of the 50 patients treated, in 3 the treatment has as yet not been completed and 4 died as a result of intercurrent infections so that only 43 are available for consideration. These 43 cases were as follows: basal cell carcinoma in 30 cases, spinocellular carcinoma in 11 cases, carcinoma in lupo 2 cases.

Since this study was instituted the patients have been observed from nine months to thirty-one months and the most up to three years. The primarily cured cases were subjected to a careful examination every three months.

The tolerability of this method of treatment was splendid. Nausea, dizziness and headaches occurred only rarely and even then did not last very long. Not in a single case was a definite roentgen burn obtained. About three weeks after the treatment has been instituted, there occurs a reaction of the irradiated tissue of a variable severity, expressed in the form of redness, swelling, and at times also a superficial ulcer formation is present. The degree and severity of this reaction varies in individual cases; while in some definite inflammatory changes are present, in others only a slight swelling and redness appear. No definite relationship could be observed by the author between the curative effect and the degree of the local inflammation. It may be stated with certainty that the reactive processes occurring on the irradiated skin must not be considered as an expression of injury of the skin but represent a physiological reactive effect to the therapeutic measures which is soon substituted by a curative effect.

In all the 43 cases, that is, in 100 per cent, a definite effect from the irradiation was obtained. A complete failure was not observed in any patient. In 70 per cent of the patients a primary cure was obtained, that is, no recurrences were observed up to three years. In the cases of basal cell carcinoma which were irradiated twice daily until a total dose of 5,000 r was given, a cure was obtained in all. The author is of the opinion that this method of treatment is just as effective as the radium therapy.—*A. Schwartzman.*

Rüsken, Wilhelm. Therapeutische Beeinflussung gliomatöser Hirngeschwülste durch Röntgentiefenbestrahlung. (Therapeutic influence of gliomatous brain tumors by roentgen irradiation.) *Strahlentherapie*, 1940, *67*, 205–218.

The patient, fifty-three years of age, became ill in 1936, developing generalized epileptic attacks presenting a picture of a jacksonian character. When admitted to the author's clinic in June, 1937, there was present a hemiparalysis of the right side of the body associated with a disturbance in speech. The patient appeared semicomatose and severely ill, complaining of severe headaches, dizziness and nausea. The eyegrounds presented no pathologic findings with the exception of congestion of the veins. Encephalography revealed a space limiting process in the left parietotemporal region. A brain puncture of this region revealed a tissue rich in cells with pathologic cell forms which was interpreted as a gliomatous tumor tissue.

After an intensive roentgen irradiation of the tumor given over five fields and each field irradiated after having been covered with an 0.5 copper filter with 2,700 r, the subjective and objective symptoms considerably decreased so that the patient could be discharged, and after his discharge he was able to work his farm. On readmission two and a half years later there developed shortly before the admission a slight aggravation of the symptoms associated with convulsions which were not present in the interval of well being. A repetition of the encephalography presented an entirely changed picture. Signs of a space limiting process were no longer present but there were present certain indications of a slight atrophic process of the brain. It was assumed that as a result of the roentgen irradiation there occurred an involution of the pathologic tissue which explained the clinical improvement. To what extent the improvement was due to involution of the pathologic tissue or to what extent it was due to the elimination of the edema or the destruction of the tumor tissue proper could not be determined on the basis of the encephalographic findings.

Roentgen irradiation of glioma patients should be carried out only after the clinical findings in the course of the disease have been carefully evaluated. This author is of the opinion that a large number of cases can be irradiated without a preceding opening of the skull. The author emphasizes the fact, however, that results could be expected only from an intensive irradiation whereby, however, all proper measures should be taken for the prevention of the unpleasant complications of the irradiation. This author is of the opinion that the so-called Coutard method of irradiation is most effective also in brain tumors.—*A. Schwartzman.*

Taylor, Grantley W., and Nathanson, Ira T. Evaluation of neck dissection in carcinoma of the lip. *Surg., Gynec. & Obst.*, Oct., 1939, *69*, 484–492.

From a tabulation of the size of the lip lesion in relationship to node metastases with and without neck dissection, the duration of the lip lesion in relation to node metastases, grade of malignancy, age of patient, metastases in lymph nodes not felt, and the size of palpable nodes in relation to metastatic involvement in cases of both primary and secondary neck dissection, the authors have drawn some very important conclusions in their analysis of the end-results. An evaluation of the data shows the following indications for neck dissection which are listed by the authors as follows:

Cases without palpable nodes or with nodes less than 1 cm. in diameter perhaps should have prophylactic dissection in highly malignant lesions and in patients who for various reasons cannot be kept under proper observation. Careful follow-up in either event is important.

Cases with lymph nodes larger than 1 cm. in diameter should be given the benefit of neck dissection as part of the original treatment but not at the same sitting as the lip treatment. The dissection should be carried out after biopsy and mouth hygiene has been done, local sepsis has been cared for and the nodes have been reappraised after healing of the primary site after excision or irradiation.

Neck dissection should not be carried out unless there is a reasonable assurance that the primary lesion has been cured. Secondary dissections may be necessary and are often successful if undertaken promptly. The border line between inoperable and operable cases is hard to define. Fixation of the nodes, extracapsular involvement and multiplicity, especially if bilateral, argue for incurability. The authors believe that only an occasional case will be helped by very radical procedures in such cases and the operative mortality is great. They have no experience with interstitial irradiation and surgery. The inoperable cases are given roentgen therapy but this in their hands has not resulted in any cures. The routine suprahyoid dissection, unilateral unless the lip lesion extends to the midline, is adequate when properly performed unless there is obvious clinical evidence of node involvement.—*P. C. Swenson.*

Meigs, Joe Vincent, and Jaffe, Henry L. Carcinoma of the cervix treated by roentgen-ray and radium. *Surg., Gynec. & Obst.*, Sept., 1939, *69*, 257–266.

This is an analysis of 70 cases from the Pondville Hospital previously reported by the authors in 1937 at the three year follow-up period and now reported at five years. The treatment given consists of a dose of 1,500–2,000 r air measurement, the total dose depending upon the rapidity with which the treatment is given. This dose is given over four pelvic fields each 8×10 cm. or 10×10 cm., two anterior and two posterior. The rays are directed obliquely at the cervix and parametrium by means of a centering device. Daily doses of 300–400 r are used, alternating the fields so that each field receives an exposure every fourth day. Roentgen rays of 200 kv. (peak) are used with 0.5 mm. Cu and 1 mm. Al filtration. The treatment averages eighteen days. At the end of that time the patient is given radium in the form of a small emanation needle placed in a 1 mm. platinum applicator. This is placed in the cervix for a total of 1,500 mc-hr., the treatment lasting about five hours. Four days later the same treatment is repeated. Little systemic reaction is obtained and no bladder or rectum irritation. No vaginal slough. This is in contrast to the old method where gold seeds were used in the periphery of the cervix and a silver cylinder in the canal. The authors compare their five year results with other clinics and they follow closely those of the Memorial Hospital and Women's Hospital of New York which are the largest series of the group. It is evident from their charts that evidence of prognostic value can be obtained, and the authors point out that it is no longer necessary to follow patients for five years before reporting

them, for the end-results at three years, if known, can be used to predict the five year result which seems to be a 15 per cent drop for most clinics. Microscopic slides are routinely studied while the patient is being treated to watch the irradiation reaction which is important from the prognostic standpoint. Biopsy should be taken before and after treatment.

The authors believe that kidney lesions due to blocked ureters with uremia are among the chief causes of death. Urological investigation is therefore important at all times since early recognition of ureteral block is obviously important.—*P. C. Swenson.*

Pemberton, John de J. Malignant lesions of the thyroid gland. *Surg., Gynec. & Obst.*, Oct., 1939, *69*, 417–430.

Seven hundred and seventy-four cases of malignant tumors of the thyroid gland were studied. The age incidence is the same as that of carcinoma elsewhere, although the occurrence in children is more common than is generally suspected. Any mass in the thyroid gland in children should be suspected of being malignant. A large percentage of these tumors originate in benign adenomas. The basal metabolic rate is of no aid in determining malignant changes. The histological criteria of the malignant tumors of the thyroid is the same as in other tissues of the body. The tumors may be classified into (1) papillary adenocarcinoma; (2) adenoma malignum; (3) diffuse adenocarcinoma; (4) epithelioma; (5) sarcoma. The papillary adenocarcinoma is distinguished by its low grade of malignancy and marked radiosensitivity and a tendency for the disease to spread into the regional lymph nodes where it may persist for years. Metastasis to these structures therefore does not necessarily argue against operation since radical removal of the primary lesion and the involved nodes in conjunction with postoperative irradiation offers a good chance for cure. The malignant adenoma is also of low grade malignancy and it has a tendency to disseminate by way of the blood stream. Since the lymph vessels are not involved until after the capsule is invaded, the presence of cervical metastases in this type has a graver prognosis. The adenocarcinomas are of a higher grade malignancy. The epithelioma and sarcomas are rare and very malignant. Metastasis occurs first to the cervical lymph nodes and then to the lungs. There is usually a paucity of clinical signs and symptoms, but recent growth, sense of pressure, and the presence of a tumor that is firmer and more nodular than the benign lesions is suggestive evidence. In 60 per cent of the cases studied a tumor was not suspected preoperatively. The fixation of the tumor, its greater malignancy and histological type are factors affecting operability. Irradiation is combined with surgery in treatment.

The operability rate was 49.1 per cent with a very low hospital mortality (1.8 per cent). If there was an associated tracheotomy or biopsy alone the mortality was 4 per cent. The author reports three, five and ten year survivals of 77, 70 and 58 per cent. The lower grade the malignancy, the more favorable the prognosis in these survivals. The author feels that much can be done for these patients and that they should be treated. He warns against a defeatist attitude.—*P. C. Swenson.*

Broders, Albert C., Hargrave, Robert, and Meyerding, Henry W. Pathological features of soft tissue fibrosarcoma. *Surg., Gynec. & Obst.*, Sept., 1939, *69*, 267–280.

One hundred and fifty-two cases were studied. The fibrogenic and cellular spindle cell sarcomata constitute two separate groups pathologically. The fibrogenic and the myxo sarcomas usually occur in older people and their prognosis is fairly good, cures having been obtained in 32 per cent. The reverse is true of the spindle cell type where cures were obtained in only 7 per cent. The malignancy of the fibrogenic and myxo sarcomas is proportional to the number of mitotic figures and giant cells the tumors contain. When the mitotic figures are the same in two tumors, the one having the most fibrogenic qualities is the least malignant. The cellular spindle cell sarcomas are highly malignant irrespective of the number of mitotic figures and should be placed in the highest grade.—*P. C. Swenson.*

MISCELLANEOUS

Smerchinich, Giovanni. Medicamenti ed accorgimenti sussidiari nella diagnostica addominale. (Auxiliary methods and drugs in abdominal diagnosis.) *Radiol. med.*, May, 1939, *26*, 424–428.

Many roentgenologists do not believe in using any drugs except the contrast medium.

The author finds it very useful to wash out the stomach with a teaspoonful of bicarbonate of soda dissolved in carbonated water. The mucus in the stomach may hide a niche or a nodule. The emptying of the stomach with a high acid content is often retarded. If the stomach contents is alkalinized there is more homogeneous irrigation of the small intestine.

The use of sulphate of magnesium is valuable in examining the colon, especially in examining the cecum.

It is not always necessary to use a very small amount of contrast medium for obtaining a good relief. Even in the stomach a good mucous membrane relief can often be obtained by giving a moderate amount of contrast and exercising pressure which spreads the barium into the folds of the mucosa.

If the image of the gallbladder is pale, the examination may be prolonged to the twentieth hour. If it is still unsatisfactory, visibility may be prolonged until the next day by giving a centigram of morphine-atropine; the patient may be allowed a light supper.

Gas may be eliminated from the colon by Haenisch's method; or a double cannula may be used for irrigation. It is a good thing to aspirate the air from the stomach in gastric examinations as otherwise the air bubble may mask anatomical changes.—*Audrey G. Morgan.*

Epifanio, Giuseppe. I neutroni in terapia. Azione di fisica nucleare. Alfaterapia profonda. (Neutrons in therapy. Action of nuclear physics. Deep alpha therapy.) *Radiol. med.*, April, 1939, *26*, 337–338.

Recent personal observation on large skin cancers and ulcerated nodular recurrences in mammary carcinomata have confirmed the superiority of irradiation with neutrons to that with gamma rays or with artifically radioactivated bodies.

The intensity and special qualities of the action of neutrons are due to mass action and therefore to the action of nuclear physics, that is the disintegration of atomic nuclei. Bodies artificially radioactivated act by means of the electrons which they emit: negative if prepared with neutrons, positive if produced with partial charges (alpha rays, deutons, protons). Artificial radioactivity is in fact a radioactivity with electrons.

The electrons do not disintegrate the nuclei but they have an ionizing action.

Probably the different quality and quantity of biological action produced by neutrons and artificially radioactivated bodies is due to these two different physical actions: disintegration of atomic nuclei and atomic ionization. Irradiation with neutrons produces alpha corpuscles and is therefore in part a deep alpha therapy.

It is hoped that in the future these two methods will be combined effectively.—*Audrey G. Morgan.*

Piccolo, Giacinto. Alcuni esperimenti sulla fissa zione del torio nei tessuti infiammatori. (Some experiments on the fixation of thorium in inflamed tissue.) *Radiol. med.*, April, 1939, *26*, 331–337.

Other authors have demonstrated that on the injection of stains there is an accumulation of the stain around skin lesions. Piccolo performed experiments on rabbits in which he used colloidal oxide of thorium for the injections. Some of the rabbits were normal and in others he had produced inflammations of the liver and the subcutaneous tissue experimentally. The protocols of the experiments are given and illustrated with roentgenograms. He found that thorium was deposited around the necrotic-inflammatory zones. In the liver the grains of thorium were deposited in the reticulo-histiocytic tissue immediately around the central necrosis. He believes this is probably due to the attraction exercised on the thorium by the reticulocytes which are very numerous in inflamed tissue.—*Audrey G. Morgan.*

Bade, Heinz. Die Allgemeinen und mittelbaren Wirkungen der Röntgenstrahlen in ihrer Bedeutung für die Behandlung bösartiger Geschwülste. (The general and indirect effects of roentgen rays and their importance in the treatment of malignant tumors.) *Strahlentherapie*, 1940, *67*, 353–423.

The author discusses the question of whether the effects of general irradiation which are indirect effectsa re as useful in the treatment of malignant tumors as direct action of the rays on the tumor itself. Some authors have claimed that this was the case.

He discusses first the clinical and humoral changes and the changes in metabolism which indicate that general irradiation of the body does have an effect on malignant tumors and

also the evidence from animal experiment that this is true. He then gives a clinical evaluation of 3,497 case histories of patients treated since 1912 for malignant tumors at the Surgical University Clinic of Kiel. He could not find in any case that there was any relationship between roentgen or radium treatment and the later development of metastases.

He then discusses his experimental work on white mice that had been inoculated with malignant tumors and then treated by general irradiation of the whole body. He also used general irradiation before inoculation in order to determine whether such irradiation prevented the "taking" of the inoculated tumors. He did not find that general irradiation with small doses increased the resistance of the animals to inoculation tumors. The life of the animals after inoculation was not lengthened by the general irradiation. He found only a slight lengthening of the latent period before the development of the tumors.

On the contrary, a marked decrease of natural immunity was brought about by total irradiations with 300 r. A number of animals that had absolute immunity as shown by the failure of several inoculations had this immunity broken down by such irradiations.

Total irradiation of inoculation tumors with a dose of 10 r a day for four weeks did not have any demonstrable effect on the tumors.

As an experiment in the prevention of tumors some mice were inoculated in both thighs. One of the thighs was irradiated before inoculation and the other was not. The irradiation had no effect on the "taking" or growth of the tumors. Some authors have reported positive results in such experiments but their inoculations were given intracutaneously or subcutaneously while in the cases reported in this article the injections were given intramuscularly. There was no difference in the histological pictures on the irradiated and non-irradiated sides. There was no greater tendency to metastasis in the irradiated than in the non-irradiated animals as shown by histological examination of the organs.

A detailed discussion is then given of whether it is possible to activate the reticulo-endothelial system by means of small doses of roentgen rays. Such an activation would be demonstrated by an increase in the so-called histiocytic foci of reaction. Careful histological examinations were made and some of the histological pictures are reproduced. Animals irradiated with 10 r did not show any increase of these foci as compared with untreated animals, nor were there any larger numbers of these foci in animals given total irradiation with small doses than in animals not irradiated at all.

On the other hand, after total irradiations with 300 r injury of the reticulo-endothelial system could be demonstrated. Only small numbers of histiocytic foci could be demonstrated in the different organs and they were small in size in comparison with those in non-irradiated animals and ones irradiated with small doses.

But large doses applied only to a small field also had no effect on the number or size of the histiocytic foci, from which the author concludes that even large doses of local irradiation do not injure the reticulo-endothelial system greatly.

He concludes, however, that the reticulo-endothelial system does play a part in the defense against tumor from the fact that the histiocytic foci in the different organs of the animals with tumor were on an average larger and more numerous than in non-inoculated control animals, and that the largest and most pronounced foci were seen in the animals that survived the inoculation longest or in which the tumors did not take.

On the basis of his own animal experiments and the clinical experience in human beings referred to in the beginning, he thinks that the action of total irradiation in malignant tumors is not very great, and is of little importance as compared with that of the direct action of the rays on the cells of the malignant tumor.—*Audrey G. Morgan.*

Bertelotti, L. Contributo allo studio della radioeccitazione. Ricerche sperimentali sul sarcoma Galliera irradiato in vivo ed in vitro. (Contribution to the study of roentgen stimulation. Experimental research on Galliera sarcoma irradiated in vivo and in vitro.) *Arch. di radiol.*, May–June, 1939, *15*, 322–333.

Arndt-Schultz' law holds that substances that have a depressive action in large doses have a stimulating action when given in small doses. There is marked difference of opinion as to whether this applies to roentgen rays. The author reviews the work of other investigators and reports his own work on Galliera rat sarcoma. He irradiated both in vitro and in vivo in order to test both the direct effects of irradiation on the cancer cells and the indirect

effects on the surrounding tissue. He gives three tables which report the exact dosage used, the duration of application and the development of the growth after thirty and fifty days, both for the sarcoma pulp irradiated in vitro and for the transplanted tumors in living rats. He did not find that the irradiation had any stimulating effect on the cancer growth in either case. The slight differences seen came within the normal variations in the growth of irradiated sarcomata.—*Audrey G. Morgan.*

Herčik, Ferd., Klusáková, M., and Zeman, F. Über die Verwendbarkeit der Alliumepidermis zu strahlenbiologischen Versuchen. (The use of onion skin for radiobiological experiments.) *Strahlentherapie*, 1940, *67*, 251–265.

Most of the experiments in exact radiobiology have heretofore been made on unicellular organisms. But it is also necessary to study the reaction of tissues to the rays, for the cell reacts to irradiation when associated with other cells quite differently than it does when isolated.

In order for a tissue to be suitable for radiobiological experiments it must be homogeneous, that is the different cells of the tissue must have the same form. And it must be possible to determine the reaction of the individual cells to irradiation as quickly and accurately as possible. It must be possible for the tissue to be irradiated not only with penetrating rays but with the less penetrating ones. The tissue must be as thin as possible and have only one layer of cells, so that its whole thickness may be penetrated by alpha rays. In addition to these special qualifications, it must have the general characteristics required of every biological object.

These conditions are all fulfilled by onion skin. It consists of a single layer of long oval cells and is well adapted for irradiation with alpha, beta, gamma, roentgen and ultraviolet rays. It can be obtained easily throughout the year. Strugger's method of isolating the epidermis is described. It is simple and reliable. The irradiation chambers for different kinds of rays are described.

Three methods have been used for determining the injury done to the tissue by the irradiation, the plasmolytic, the erythrosin and the fluorescence methods. These are described. So far the sensitiveness of the tissue has been determined accurately only to alpha rays. The half-value dose of the tissue is $34.10^{7}\alpha \cdot mm^{-2}$; this dose corresponds to 5.10^{5} r. The time course of the injury by the rays, the sensitiveness of individual skins and the time, space and temperature factors are discussed. The influence of the number of cells irradiated on the course of the survival curve is also determined.—*Audrey G. Morgan.*

Abele, Adolf. Versuche mit rhythmischer Bestrahlung von Eiern der Drosophila melanogaster Meig. (Experiments with rhythmical irradiation of eggs of *Drosophila melanogaster* Meig.) *Strahlentherapie*, 1940, *67*, 293–306.

A great deal of effort has been expended in determining the best methods of giving roentgen irradiation. Concentrated radiation may be given at a high intensity for a short time or protracted radiation at a lesser intensity over a longer period. It has also been claimed that rhythmical, discontinuous irradiation is more effective than continuous irradiation.

The author tested these different methods of irradiation on the eggs of *Drosophila melanogaster*. The flies were allowed to lay their eggs for two and a half hours and then stopped. A half hour later the eggs were irradiated. They were said to be twice as sensitive to irradiation at the end of three hours after the beginning of laying as six hours after.

It was found that continuous irradiation with 150 r did not show any difference in effect whether given at the rate of 23.7 to 47.6 r per minute or at the rate of 95 r per minute. A comparison of the effect of continuous irradiation of 150 r with a rhythmical irradiation with the same dose at intervals of 1/13 to 1/200 second did not show any differences.—*Audrey G. Morgan.*

Peukert, Lothar, and Koehler, Hans. Untersuchungen der sensibilisierenden Wirkungen von Teerpräparaten auf die Haut bei Bestrahlung mit Ultraviolett- und Grenzstrahlen. (Studies of the sensitizing action of tar preparations on skin irradiated with ultraviolet and grenz rays.) *Strahlentherapie*, 1940, *67*, 266–285.

Experiments in preliminary treatment of the skin with tar preparations before irradiation with ultraviolet rays and Bucky's grenz rays are reported. It was found that the coal tar preparations are better adapted for this purpose than wood tars. They are effective in the following sequence: Pix lithanthracis, liantral,

liantral-ichthynat, sulfanthrem, Liq. carbonis detergens, Ol. Rusci and balnacid.

With both ultraviolet and grenz-ray irradiation the parts of the skin treated with tar reacted more sensitively to the irradiation than the untreated parts. The threshold value before the beginning of erythema was decreased and the gradation curve was steeper, that is the erythema began sooner and increased more rapidly on the parts of the skin treated with tar.

The possible causes of this sensitizing action of tar are discussed. It seems that coal tars, even in the thinnest layer, are impermeable to these forms of light and that the irradiation is for the most part absorbed. The greater part of the tar applied to the skin is absorbed so that in addition to the action of the rays there is a longer wave irradiation from the absorbed tar, depending on the absorptive capacity of the skin, so that the reaction of the skin to long wave irradiation is increased. It will require further experimentation to show to what extent still other chemical-biological processes are brought into action on the cells and vessels by the action of the tar and to what degree these are responsible for the sensitizing action. —*Audrey G. Morgan.*

Zaffiro, Edoardo. La ricerca e la localizzazione radiologica dei proiettili con speciale riguardo ai metodi piu moderni. (Roentgen search for and localization of projectiles, with special reference to the most modern methods.) *Arch. di radiol.*, Jan.–Feb., 1940, *16*, 36–66.

The localization of foreign bodies by means of roentgen examination dates back to the very discovery of the rays. But constant improvements have been made in methods. Localization is yet by no means perfect and depends on the knowledge and skill of roentgenologist and surgeon and their close collaboration more than on the apparatus or the methods used.

Roentgen localization of foreign bodies is vastly more difficult in war than in peace because of the multiplicity of the wounds and the surroundings in which the work has to be carried on. It is still further increased by the fact that some modern projectiles are not opaque to roentgen rays; aluminum for instance is almost as transparent as soft tissue.

There are two chief methods of roentgen localization, the roentgenoscopic and the roentgenographic. In the advanced war zone where rapid action is necessary and it is difficult to transport apparatus the author believes that roentgenoscopic methods are to be preferred. Roentgenoscopy is still more useful in war today than ever before, because of the great increase of artillery projectiles and the use of bombs dropped from airplanes.

Sometimes it is necessary to have recourse to methods which depend more or less on chance, such as those of crossed axes, of puncture or the anatomical and functional methods which are so valuable when associated with geometrical ones. Sometimes methods of precision can be used such as those of Haret, Patte, Strohl, Mazérès and Baese, which are not only rapid but furnish practically exact data without the necessity of complicated calculations or drawings and without the necessity of moving the wounded man. Those of Patte, Strohl and Mazérès have the advantage of not requiring any special apparatus but they can be improvised anywhere. The perforated screen methods of Hirtz and Ghilarducci and that of Luisada do not meet the modern requirement of protection from the rays and Hirtz' method requires much skill and care and a great deal of time.

Among the methods based on movement of the tube that of Furstenau-Weski is the simplest. Stereography is valuable as it furnishes both anatomical and geometrical data but it requires a great deal of practice. The method of serioscopy may be used even in the field because of the simplifications devised by Grandgérard and Karcher. Roentgenoscopy, however, remains the method of choice at the front. It is the only method of examining a large part of the body when multiple projectiles are suspected or when it is necessary to find a projectile at a long distance from the entrance wound. The methods of roentgenoscopy and roentgenography supplement each other under peace conditions.

Descriptions and diagrams are given of the various methods mentioned.—*Audrey G. Morgan.*